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# UNITED STATES NAVY Medical News Letter

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*MEDICAL NEWS LETTER*

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*Policy*

The U.S. Navy Medical News Letter is basically an official Medical Department publication inviting the attention of officers of the Medical Department of the Regular Navy and Naval Reserve to timely up-to-date items of official and professional interest relative to medicine, dentistry, and allied sciences. The amount of information used is only that necessary to inform adequately officers of the Medical Department of the existence and source of such information. The items used are neither intended to be, nor are they, susceptible to use by any officer as a substitute for any item or article, in its original form. All readers of the News Letter are urged to obtain the original of those items of particular interest to the individual.

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FRONT COVER: NAVAL AEROSPACE MEDICAL INSTITUTE. The U.S. Naval School of Aviation Medicine was founded in 1939 but was renamed the Naval Aerospace Medical Institute 18 August 1965. Formal research began in July 1940 when scientists, under joint Navy and National Research Council sponsorship, began investigations on methods of pilot selection. The present research laboratory opened in January 1943 and is located at the Naval Aviation Medical Center in Pensacola, Florida. Research is conducted in the fields of biochemistry, biometrics, cardiology, medical electronics, neurophysiology, acoustics, physical chemistry, physiology and psychophysiology. NAMI's mission is to provide training of aviation medical personnel and to conduct research in aviation and space medicine, aviation psychology and allied fields. The Institute evaluates aeromedical equipment, supports the Naval Air Training Command in the selection, indoctrination, and instruction of nonmedical aviation personnel, and provides professional and consultation services in aviation medical matters as required. The vigorous research, development, test and evaluation program in aviation and space medicine supports the Bureau of Medicine and Surgery, Naval Air Systems Command, the National Aeronautics and Space Administration, and other Federal agencies. Over the last few years NAMI has successfully completed numerous studies in aviation and space medicine, many of which are still continuing. Studies involving improved aviation training methods, and relating to the varied stresses in manned space flights, are expanding the nation's knowledge in many areas previously little explored. Among the many noteworthy individual scientists who have worked in the Institute and its predecessor agencies over the years Captain Ashton Graybiel of the Navy's Medical Corps has been a leading figure.

The issuance of this publication approved by the Secretary of the Navy on 4 May 1964.

# THE NATURAL HISTORY OF CONGENITAL MALFORMATIONS*

*Vergil H. Ferm, MD PhD, Chairman, Department of Anatomy and Cytology, Dartmouth Medical School,* *Bulletin of the Geisinger Medical Center, 19(3):83–86, August 1967.*

Congenital malformations represent an increasingly important part in the total load of human disease. Approximately 7 percent of human term newborns suffer from some aberration of development which will necessitate substantial and prolonged medical attention and/or shorten their expected life span. The actual human malformation rate is indeed much greater than this, for the incidence of developmental anomalies in abortuses and stillbirths is remarkably high. The tremendous psychological burden and long-term medical care and cost to parents and other members of the family as well as to the affected individual are incalculable. Thus, if we can define the natural history of specific malformations, we should be able to suggest some rational reasons for their etiology and, hopefully, to begin to offer reasonable counseling to parents and to others concerned about these types of disabilities.

The natural history of a disease process must consider a variety of interrelated factors which bear directly upon the ontogeny of the disease. Broadly speaking, these can be characterized by two very general headings—heredity and environment. Obviously, each of these can be further subdivided into many subheadings. For the sake of simplicity the following outline appears to be the most manageable and most informative at the present time.

## Influence of Hereditary Factors in Congenital Malformations

From both clinical observations and animal experimentation it is now known that genetic factors play a significant role in the etiology of certain congenital malformations. In some malformations such as ectodermal dysplasia, cleft lips, and central nervous-system lesions the importance of hereditary factors is quite clear. In other malformations such as congenital heart disease, vascular abnormalities, and tracheoesophageal fistulas genetic factors are suspected but not proved. Recently a whole spectrum of human developmental malformations have been shown to be due to minor changes in the chromosome complements of individuals. These chromosomal aberrations have been linked directly to cases of mongolism (Down's syndrome), Turner's and Klinefelter's syndromes, and many others. While not true genetic factors in the strict sense of the term, these chromosomal aberrations emphasize the marked importance of a balance in the quantitative amounts of genetic material in the regulation of normal development. The most remarkable example of a genetic role in mammalian malformations is that of the Disorganization (Ds) mutant gene in the mouse. In this condition all organ systems of the surviving heterozygotes are severely malformed, demonstrating a wide spectrum of congenital anomalies. Certainly, as time goes on and the methodology of genetic analysis becomes more sophisticated, a greater proportion of those developmental malformations whose etiology at the present time is not clear will prove to have an important hereditary component.

## Influence of Environmental Factors in Congenital Malformations

At the other end of the spectrum are those malformations which are due to pure accidents of sudden environmental change during critical stages of embryogenesis. Rubella infection, thalidomide, and x-irradiation are the classical examples of environmental factors causally related to human congenital anomalies. Even in these instances it is not altogether certain what role the underlying genotype plays in the incidence and expression of the developmental pattern. Experimental evidence in mice, for example, reveals that cortisone treatment of the mother will produce different incidence rates of

*Presented to Staff Meeting of the Geisinger Medical Center, January 9, 1967.

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cleft palates in her embryos depending upon the specific strain of mice used. The figure reveals the multitude of environmental factors which may affect the development and differentiation of the embryo during critical stages of organogenesis.

Thus it becomes necessary to try to delineate the many factors which enter into the ontogeny of developmental malformations. Experimental teratology has provided a method for initial and helpful insights into many of these problems. In such experiments both the genetic and the environmental components can be altered at will, and various factors in pregnancy and embryogenesis can be studied under well controlled conditions.

The golden hamster is an ideal animal for the study of many problems of embryonic development. It breeds readily and under conditions which permit the determination of exactly timed matings. It has large litters and its gestation period is extremely short (16 days). The critical stages of organogenesis in this animal occur within a 24-hour period, from the eighth to the ninth day of gestation. In this period almost all of the organ systems undergo differentiation. This short interval corresponds to the period from the 18th to the 28th day in human gestation, a period when organogenesis proceeds almost to completion and during which environmental teratogens would be most effective in disrupting the orderly sequence of organ and tissue formation.

From our studies utilizing this experimental model a few important principles pertaining to embryonic development have emerged. It is apparent that these might well apply to human development and are areas in which further investigation should develop.

First, it is obvious that the placental membrane plays an important part in embryonic development. This dynamic membrane, which represents the sole frontier of the developing embryo, can transmit, block, or delay the transfer of various substances from the maternal system to the embryonic system. In experimental studies with various viruses, for example, it has been shown that the mumps and herpes-simplex viruses are blocked from transfer to the fetus even though they proliferate to a marked degree within the placenta proper. On the other hand, the smaller rat (RV) and H–1 viruses penetrate the placenta easily and reach the embryo where they proliferate readily. Even so, infection of the fetus does not necessarily mean fetal disease nor congenital malformations since the RV produced no known fetal disease. H–1 virus, however, causes a wide range of anomalies in these hamster embryos with histopathological evidence of viral activity. Our knowledge concerning the placental transfer of viruses, hormones, and other potentially teratogenic compounds in the pregnant human patient is meager. Only recently, the demonstration of the surprisingly high frequency of fetal red blood cell transfer to the maternal circulation attests to the relative lack of integrity of this membrane. Further studies on placental permeability *in vivo* and *in vitro* are needed to identify those agents which are potential teratogens.

Secondly, it is no longer correct to say that all teratogens will cause the same malformation if embryos are insulted at identical times in development. There is accumulating evidence that there is a specific teratogen: organ response. In human malformations this is best demonstrated by the rubella virus: patent ductus arteriosus and the thalidomide: phocomelia syndromes. There are other examples of this, but these will suffice to emphasize that there is some characteristic of the embryonic tissue which responds rather specifically to a particular teratogenic insult. In our experimental model the injection of lead salts during gestation produces a highly specific malformation of the tail-bud and sacral vertebrae in the embryos. The injection of dimethylsulfoxide (DMSO) will, however, produce no tail malformations but rather a high incidence of anterior axial lesions, such as exencephaly. One promising approach to this problem will be the study of the effects of various teratogens on cell organelles, using the electron microscope in an attempt to differentiate those intracellular distinctions which exist to produce this rather specific teratogen: organ effect.

Thirdly, certain teratogenic stimuli can be markedly enhanced by manipulation of environmental factors which are not teratogenic in themselves. These environmental changes are called *proteratogens*. Certainly these are the most subtle and most difficult of all problems to unravel in human and experimental teratology. The recent observations of human epidemics or clusters of mongolism and spina bifida need further acute observation and attention. Experimental evidence reveals that changes in environmental temperature, which in itself is nonteratogenic, dramatically increase the teratogenic effect of Vitamin A. The problems inherent in studying these relationships are quite apparent. For example, it is very likely that even the expression of genetically caused human congenital malformations may be greatly

influenced by very subtle changes in the environment during gestation.


Summary

Congenital malformations represent a significant factor in the load of human disease. Certain of these malformations represent purely genetic phenomena, others purely environmental, while the vast majority are probably related to subtle influences of environmental changes on a specific genotype. Placental permeability and the specificities of the responding embryonic systems also play important roles in the etiology of mammalian malformations.


(The omitted figure and references may be seen in the original article.)

# MELIOIDOSIS PNEUMONITIS

## *ANALYSIS OF NINE CASES OF A BENIGN FORM OF MELIOIDOSIS*


*LTC Murray Spotnitz, MC, USA; CPT Jerome Rudnitzky, MC, USA; and MAJ Jacques J. Rambaud, MC, USA, JAMA 202(10):950–954, Dec. 4, 1967.*


Melioidosis has been known as a highly fatal bacterial infection of tropical areas. Epidemiological studies indicate that the disease is much more common than previously suspected because a high incidence of asymptomatic infections was found among natives of the endemic areas. In nine patients in whom the infection was confined to the lungs, the clinical manifestations closely mimicked pulmonary tuberculosis with upper-lobe infiltration and cavitation. The course was subacute, the patients had a productive cough, blood-tinged sputum, chest pain, fever, chills, weight loss, and anemia. This form of the disease showed an excellent response to appropriate antibiotic therapy. Isolated pulmonary melioidosis is a relatively benign disease and does not have the same prognosis as the septicemic form.

Melioidosis has been considered a rare, highly fatal, infectious disease endemic to tropical areas of southeast Asia, the Caribbean, and northern Australia. The causative organism, *Pseudomonas pseudomallei,* is a gram-negative, bipolar-staining, motile bacillus which leads a saprophytic existence in nature. Since this hardy bacillus is so widespread in the soil and stagnant waters of the Malay peninsula, the opportunity for man to acquire an infection must be great. It is, therefore, a paradox that cases of melioidosis in humans have remained so rare.

Recent studies have suggested a solution to this puzzle. Serologic surveys have revealed abnormal results in 7% to 10% of the adult male population in endemic areas. Since animal experiments indicate the serological titer does not remain elevated indefinitely after an infection, a high percentage of the natives must survive unrecognized or asymptomatic encounters with the infective organism. It is, therefore, probable that melioidosis is, instead of being rare, one of the major diseases of southeast Asia, but only occasionally causes diagnosed illness.

By analogy with other diseases which are contracted from soil saprophytes and cause a high incidence of asymptomatic infections in man, eg, coccidioidomycosis and histoplasmosis, it would be expected that there are many relatively mild melioidosis infections for every fatal case that is diagnosed.

The clinical features of nine cases of pneumonitis caused by *P. pseudomallei* are described in this report. That there are characteristic manifestations of melioidosis pneumonitis has not been previously stressed. It is, therefore, possible that many patients have been cured of this form of the disease without the correct diagnosis being made and that a relatively mild pneumonitis rather than the highly


From the Pulmonary Disease Service, Valley Forge General Hospital, Phoenixville, Pa. Dr. Spotnitz is now with the Department of Medicine, Maricopa County Hospital, Phoenix, Ariz.



Read before the Section on Military Medicine at the 116th annual convention of the American Medical Association, Atlantic City, N.J., June 19, 1967.



Reprint requests to 51 E Hayward, Phoenix, Ariz. 85020 (Dr. Spotnitz).

fatal septicemia is a common way for melioidosis to present itself.

## Clinical Observations

From January through December 1966 nine patients with pulmonary melioidosis were admitted to Valley Forge General Hospital. Six were referred from military hospitals in Vietnam and three from military hospitals in the United States. In eight patients, the referral diagnosis was pulmonary tuberculosis, and in one it was granulomatous disease of the lung due to unknown cause.

The patients were all male soldiers ranging in age from 20 to 40 years. Eight were white, and one was Negro.

None of the patients had been wounded. All had been in previously good health and, except for the stress of combat, had no detectable cause for having altered resistance to infection.

They came from unrelated military units and had not been in contact with each other. Their military occupations were also varied, ranging from clerk to helicopter gunner to combat infantry man.

Two of the patients became ill after returning to the United States. One had been in Laos from 1959 to 1960 and had not left the United States since then. In 1962 a routine chest roentgenogram revealed a calcified nodule at the apex of the right lung. Yearly chest roentgenograms were unchanged until December 1965 when a large cavitary lesion was noted in the upper lobe of the right lung in an area remote from the original abnormality. The other patient was being processed for discharge from the Army a few days after returning from Vietnam when a chest roentgenogram revealed a cavitary lesion in the superior segment of the lower lobe of the right lung.

The onset of the disease was sudden in only one patient. He became ill with a temperature of 104 F (40 C), shaking chills, chest pain, and marked fatigue. This patient was admitted to a hospital in Vietnam where therapy was started within hours of the first symptoms. Two patients were well when the diesease was discovered by fortuitous chest roentgenograms. Before the diagnosis was established and therapy begun they both became ill with fever and systemic symptoms. In the other patients, the symptoms were tolerated from several days to as long as three months before hospitalization.

The major symptoms and signs were fever (eight patients), purulent sputum (six patients), hemoptysis (three patients), chills (five patients), chest pain (seven patients), and weight loss (nine patients). The maximum temperatures recorded were as follows: 101 F (38.3 C), one patient; 102 F (38.9 C), one patient; 103 F (39.4 C), three patients; and 104 F (40 C), three patients. In six patients the fever was high and remittant with spikes recurring almost daily until therapy was begun. One patient never had a fever during the course of the illness. This patient had chest pain for three months, but did not seek medical aid until he coughed up a small amount of blood. The hemoptysis did not recur, but the chest pain became very severe and required narcotics for control. This symptom dramatically subsided after appropriate antibiotic therapy was begun. Another patient had a temperature elevation of 101 F (38.3 C) on the day he was admitted to the hospital in Vietnam. The fever subsided without therapy and did not recur. A third patient's temperature spiked to 102 F (38.9 C) on the day of admission to our hospital. He continued to have low-grade elevations to 100 F (37.8 C) until therapy was started.

Three of the patients had no cough. The others complained of a productive cough with purulent appearing sputum. One of the patients who had a chronic cigarette cough noted an increase in sputum production when he became ill. In three patients the sputum was blood streaked. No gross hemoptysis was observed.

Five of the patients had severe shaking chills. Chest pain was described as pleuritic or as dull and aching in character. When this symptom was present, it was always prominent and often led the patient to seek medical aid. All of the patients lost considerable weight during the illness. This ranged from 5.4 to 22.7 kg (12 to 50 lb) with a mean loss of 12.7 kg (28 lb).

One patient had a severe sore throat associated with the chest symptoms. The pharynx was red, but no pathogen was cultured from it. This symptom subsided along with the others after antibiotic therapy was begun.

None of the patients appeared to be critically ill despite the loss of weight. Five of the patients had rales in the area of the pneumonitis. One patient had diffuse rhonchi. A patient who had lost 22.7 kg (50 lbs) had decreased sensation and paresthesias of the lower extremities. It was felt that he had peripheral neuritis secondary to a nutritional deficiency. The patient has shown consid-

erable improvement since recovery from the pulmonary illness. No patient had hepatomegaly, splenomegaly, or peripheral lymph-node enlargement.

Laboratory data are listed in the Table. The white blood cell count (WBC) and differential were variable and showed no correlation with the severity or acuteness of the illness. Three patients had a normochromic, normocytic anemia. They all had been ill for at least two weeks before therapy was instituted. The hematocrit reading returned to normal after antibiotic therapy. The erythrocyte sedimentation rate was elevated in all patients on whom the test was done. This rate also promptly returned to normal after therapy. Urinalysis, blood urea nitrogen level, blood glucose value, and liver function tests were normal in all patients.

Chest roentgenograms showed a striking resemblance to those seen in pulmonary tuberculosis: right upper-lobe disease (four patients), left upper lobe (two patients), right upper lobe and middle lobe (two patients), right lower lobe (one patient), and presence of cavitation (seven patients).

The patient with lower-lobe disease had a cavity in the superior segment, another favored location for tuberculosis. In one patient the initial lesion appeared as a cavity in the right upper lobe. Treatment was delayed for over a month during which time the middle lobe became involved.

Seven patients had pulmonary cavitation. This was always present on the first roentgenogram taken, even in the patient whose illness was so acute that he was hospitalized on the day of onset. The cavities tended to be thin-walled and varied in size from 1 to 4 cm.

LABORATORY FINDINGS

| | Range | Mean |
|---|---|---|
| WBC, No./cu mm | 8,700-20,000 | 12,130 |
| Neutrophils, % | 45-85 | 70 |
| Hematocrit value, % | 34-normal * | ..... |
| Erythrocyte sedimentation rate (7 patients), mm/hr | 18-57 | 39 |

*Hematocrit values: 34% (two patients), 36% (one patient), above 42% (all others).

Nodular infiltration was present in a lobar or segmental distribution. Except possibly for the thinness of the cavity walls and the absence of pleural reaction, the chest roentgenograms could not be differentiated from those seen in pulmonary tuberculosis.

The diagnosis of melioidosis was established in all patients by repeatedly culturing *P. Pseudomallei* from the sputum and obtaining abnormal results from serological tests. In some of the patients, blood, stool, and urine specimens were cultured and found to be negative.

All patients had diagnostic elevations of the melioidosis hemagglutination test, and eight had positive results for complement fixation tests as well. In seven patients, serial serological studies were performed over several months. Two patients eventually showed a marked drop in titer while the rest continued to have very high titers even though the chest roentgenograms had improved and they remained well.

Response to antibiotic therapy was dramatic, but therapy had to be prolonged or relapse might occur. One patient who became ill in Vietnam was given three short courses of tetracycline therapy. Each time the drug was discontinued, the fever recurred. After 30 days of continuous antibiotic therapy, the chest roentgenogram had cleared and there were no further relapses.

Another patient was given tetracycline, 1 gm daily, when the diagnosis of pneumonitis was made in Vietnam. When the fever persisted, the dose was raised to 2 gm a day, and his temperature returned to normal. Because the upper-lobe infiltration failed to improve, the patient was evacuated with the diagnosis of tuberculosis. The chest roentgenogram showed almost complete clearing by the time he reached our hospital. Sputum cultures were then repeatedly positive for *P. pseudomallei* despite roentgenographic resolution of the disease.

Two patients who had mild systemic symptoms were given a two-week trial of kanamycin sulfate, 1 gm daily. Neither showed any response on the chest roentgenogram although one patient's cultured sputum specimen became negative. The pulmonary lesions subsequently resolved on tetracycline therapy.

All the other patients responded rapidly to tetracycline therapy. Treatment with 3 gm a day was given for a minimum of 30 days or until the cavities had closed and the chest roentgenogram was normal or revealed only stable residual scars.

Follow-up as long as 14 months has indicated that the disease has been controlled.

## Comment

The clinical classifications of melioidosis are subclinical (only abnormal results of serological study), pulmonary, septicemia, and extrapulmonary.

Based on the previously mentioned serological surveys, there must be thousands of people in the

endemic areas who have survived subclinical infections with melioidosis. Subclinical infections are not always benign, however. Thus, an indolent pneumonitis due to *P. pseudomallei* developed in one of the patients reported here five years after he returned from Laos. Guillermand et al reported a case in which melioidosis caused recurrent abscesses of the lung several years after the patient left Vietnam. Both of the patients noted above survived, but two other patients with late relapses died.

If McDowell and Varney's patient contracted melioidosis in Panama, the diagnosis was not made until 17 years later. This would be the longest latency on record.

That fatal cases of melioidosis are really rare and not merely overlooked was shown in an autopsy series from Kuala Lumpur, Malaya, which revealed an incidence of 1.5 per 1,000 deaths.

Although very few cases of melioidosis have been diagnosed during the present conflict in Vietnam, it is likely that subclinical infections have occurred and that occasional patients with late relapses will be seen in this country. Because of the short residence in the endemic area, American soldiers should have less opportunity than the natives to become infected. Only 1.1% of 372 unselected patients admitted to Valley Forge General Hospital from Vietnam had significant elevations of the melioidosis hemagglutination test and no clinical evidence of infection.

Pneumonitis due to *P. pseudomallei* has characteristic, albeit nondiagnostic, manifestations. The diagnosis is strongly suggested if a patient has been in the endemic area and if pneumonitis develops which involves an upper lobe with early cavitation. The subacute course with symptoms of chest pain, cough, blood-tinged sputum, weight loss, fever, and anemia bears a striking resemblance to pulmonary tuberculosis. Recurrent attacks of shaking chills is an important differential point favoring melioidosis.

Other authors have not attempted to separate melioidosis pneumonitis as a disease, which is readily responsive to therapy and has a good prognosis, from the very serious melioidosis septicemia. That these cases are probably common but not reported is suggested by a recent case report by Vietnamese physicians in which they recount a case—much like those described here—in which the patient had the typical manifestations of melioidosis as seen by native physicians in Vietnam.

The diagnosis of melioidosis pneumonitis is established by culturing *P. pseudomallei* from the sputum. The organism is aerobic, grows well on ordinary media, and has a characteristic wrinkling of the colonies after a few days. Definitive identification is made by demonstrating motility and fermentation of sugars. Since many bacteriologists are unfamiliar with this bacillus, it has been confused with *Klebsiella* and *P. aeruginosa* or even ignored as a contaminant when it was not in pure culture.

Hemagglutination and complement fixation tests tended to remain at high levels in some of the patients over several months. No prognostic significance could be attached to this finding, as all the patients have remained well regardless of the titer of the serologic tests. Since patients with subclinical melioidosis have abnormal results in serological tests, one should be wary of attributing current symptoms to this disease in the absence of bacteriologic confirmation. The positive results of a blood test may signify a past, rather than present, encounter with the illness.

The septicemic form of melioidosis has been most commonly recognized. Whitmore reported on 38 cases in his original descriptions of the disease. The blood stream was invaded and multiple small abscesses developed throughout the lungs, liver, spleen, and other organs. Even though the patients might have severe gastrointestinal symptoms, the gastrointestinal tract was consistently spared. Although fever and wasting were constant features, the clinical manifestations were extremely variable depending on which organ or organs bore the brunt of the infection. Alain et al could do no better than to classify their 28 patients into acute, subacute, and chronic forms.

Of the 83 cases reviewed before the antibiotic era, only two patients survived the septicemia. Even with the availability of effective antibiotic therapy, this is still a very serious infection.

In contrast to the patients with melioidosis pneumonitis who were in previous good health, diminished general resistance is an important factor in septicemia. Many of Whitmore's patients were debilitated morphine addicts. The patients from Australia had diabetes mellitus, renal disease, liver disease, pregnancy, and extreme youth as predisposing factors. In Alain's series 12 patients had another significant illness; three had a concommittant infection with another bacterial organism, and five had had surgical trauma.

The importance of good general resistance is emphasized in our patients, many of whom were ill for weeks before therapy was begun, yet the disease was contained in the lungs and septicemia did not occur.

Localized extrapulmonary forms of melioidosis may be blood borne or local. Cases of osteomyelitis, arthritis, and some subcutaneous abscesses seem to be examples of the blood borne form. *Pseudomonas pseudomallei* has been isolated from suppurating wounds in patients who remained afebrile and had no systemic symptoms. In these cases, it is reasonable to assume that the infection was introduced from without.

The antibiotic sensitivity pattern of strains of *P. pseudomallei* is variable enough to justify in vitro sensitivity tests for planning effective therapy. Most of the strains of our patients were sensitive only to tetracycline and derivatives, chloramphenicol, novobiocin, kanamycin, and sulfonamides.

Experimentally chloramphenicol is the most effective antibiotic available. In three of our patients, the organism was resistant to chloramphenicol. Therapeutic results were so dramatic with tetracycline in these patients, that there seemed little justification for using the more potentially dangerous antibiotic. Although kanamycin sulfate showed promise from in vitro tests, the results in the two patients to whom it was administered were disappointing.

One of our patients confirmed the experimental results which indicated that high doses of tetracycline are required for a favorable effect. He did not respond to 1 gm per day, but promptly became afebrile when the dose was increased. We have routinely used 3 gm of tetracycline a day administered orally.

As French physicians have shown us, short courses of antibiotic therapy are dangerous, since relapse with resistant organisms may occur. Therapy has, therefore, been continued for at least 30 days in all our patients or until cavities had closed and the chest roentgenogram showed stable residuals. Fortunately, the one patient who received several short courses of tetracycline therapy before the diagnosis was established, continued to have sensitive organisms.

In the septicemic form, the poor prognosis justifies greater risks, and large doses of chloramphenicol for prolonged periods are indicated. Chambon states that there is a synergism between chloramphenicol and the tetracyclines, so this may be a desirable combination in severe cases.

As the story of melioidosis unfolds, striking similarities to histoplasmosis and coccidioidomycosis become apparent. These diseases are caused by highly contagious soil saprophytes. The first patients had severe overwhelming illnesses. Epidemiological studies subsequently showed that a high incidence of asymptomatic infections had occurred among natives of endemic areas. Occasional late relapses occurred among individuals who had apparently withstood mild or asymptomatic infections. In melioidosis, as in the fungal diseases, a relatively mild pneumonitis is a common clinical manifestation of the illness.

Generic and Trade Names of Drugs

Chloramphenicol—*Chloromycetin, Cylphenicol, Tega-Cetin.*
Tetracycline—*Achromycin, Panmycin, Tetracyn.*
Kanamycin sulfate—*Kantrex.*

(The figures and references may be seen in the original article.)

## FAT EMBOLISM IN TRAUMA

*Vladimir Palmovic, MD, and James R. McCarroll, MD, New York,*
*Arch Path 80(6):630–635, December 1965.*

Since the forensic pathologist is often expected to determine the sequence of events in cases of traumatic death based solely upon autopsy evidence, knowledge of both antemortem and postmortem physiologic changes is essential in the performance of his work. Among the many autopsy findings which are helpful in this determination the presence and degree of fat embolization may be of

Submitted for publication Sept. 10, 1965. From the Office of the Chief Medical Examiner of the City of New York; the Department of Forensic Medicine of New York University School of Medicine (Dr. Palmovic); and the Division of Epidemiologic Research of the Department of Public Health of Cornell University Medical College (Dr. McCarroll). Reprint requests to 1300 York Ave., New York, NY, 10021 (Dr. McCarroll).

considerable importance. The present study was undertaken to determine (1) the time at which fat entered the circulation, (2) the degree of fat embolization associated with various types of injuries, (3) the relation of the amount of fat to survival time, (4) the time of appearance of fat embolization in the systemic circulation, (5) the role of fat embolization as a cause of death, and (6) whether fat embolism may be produced by closed chest cardiac massage.

## Material and Methods

Because fat embolization is mainly a complication of injury the case material studied consisted of persons autopsied, in the Office of the Chief Medical Examiner of New York, whose deaths were due to various types of trauma. A total of 300 accident victims were studied whose deaths had resulted from automobile accidents, airplane crashes, falls, occupational injuries, and other types of mechanical trauma. A second group of 131 persons dying of causes other than mechanical trauma, including chronic alcoholism, diabetes, poisoning, etc, served as a control group. All autopsies were personally performed by one of us, through the cooperation of Dr. Milton Helpern, Chief Medical Examiner of the City of New York. At each autopsy, sections from each lobe of the lung, and sections from peripheral and central portions of brain and kidney were obtained. The tissue was fixed in Formalin solution and frozen sections prepared. Tissues were cut at 15$\mu$ intervals except for the lung which was cut at 20$\mu$. The sections were stained with hematoxylin and by either Sudan III or the Fettrot method for demonstrating fat globules. In some cases the tissue was embedded in paraffin and standard hematoxylin and eosin staining was used.

The degree of fat embolization was estimated microscopically and graded on a scale of 1+ to 4+ fat ranging from occasional intravascular fat globules to a massive lipid embolication. Actual counting of emboli was not used since distention of tissue, especially lung, during preparation renders this method unreliable. Repeated examination of unidentified sections by both the same and different examiners yielded consistently reproducible results.

## Results

The age distribution reached a peak at the sixth decade, and a smaller peak occurred in children below the age of 10. There was a high correlation between degree of injury and survival time as might be expected. Thirty-four percent of the injured were found dead at the scene or died during transportation to a hospital. Twenty percent died within the first six hours, 63% within 12 hours, and 73% within 24 hours after the accident. The greatest mortality was among those with multiple injuries especially within the first 12 hours after the accident. Among the cases with only one fracture many had a fracture of the skull and injury to the brain resulting in the large number of deaths in this group in the first 24 hours. Death after five to ten days was usually due to complications such as thrombotic embolism or to brain injury and traumatic intracerebral hemorrhage.

## Degree of Fat Embolism by Survival Time

Only 20% of those who died immediately did not have evidence of fat embolism, and the remaining 80% had embolism of varying degrees. About 15% had severe fat embolism (3+) despite their sudden death. Of course it is probable that some of those found dead at the accident site, or who were dead on arrival at a hospital, survived the accident for a short time and in these cardiac action may have persisted for a few minutes.

In those living up to six hours after their accident fat embolism was found in 96%, and 12 hours after the accident there was not a single case without fat embolism regardless of type of injury. After 12 hours the percentage without fat embolism increases slowly as survival time lengthens and fat is slowly eliminated from the circulation. The curve of massive embolism rises sharply in the first 12 hours and the peak is found between six and 24 hours after injury.

## Fat Embolism by Type of Injury

The type of injury is also an important factor in determining the degree of fat embolization. Massive fat embolism was never found in cases with only soft tissue injury, but this did occur in 26% of those with one fracture, and was frequent with multiple injuries (44%). Moderate fat embolism was observed with all types of trauma.

## Fat Embolism by Age

The age of persons injured is not important in the appearance of fat embolism, but there is a difference in the amount of fat with age. Older persons tend to have larger amounts of pulmonary

fat emboli, whereas children more often have lesser amounts.

### Bone Marrow Embolism

In a group of 180 cases in which a special search for bone marrow emboli was made 21 (11.8%) had bone marrow embolism in the lungs. Bone marrow embolism is rarely a massive phenomenon and undoubtedly would be observed more frequently if more sections were made. In only one case of abdominal trauma with rupture of liver and inferior vena cava was a piece of liver tissue seen in a pulmonary vessel.

### Systemic Embolization

In the same series of 180 cases studied for the presence of bone marrow emboli systemic embolism was found in 18 (10%). Fat embolism in the brain without demonstrable embolism in the kidney was observed four times, and in eight cases there was embolism in the kidney without simultaneous embolism in the brain. In seven cases (3.8% of the total series) massive systemic embolism was found and was considered to be the cause of death. Thus, of those sustaining systemic embolization, 38% were considered to have died of this cause. In four of these seven there were clinical signs of embolism with petechial hemorrhages of the brain and conjunctiva as well as coma. These four persons died two hours, 20 hours, two days, and eight days after injury. All had cerebral coma without evidence of direct injury to the brain. In the three other cases there was no evidence of petechial hemorrhage. Those persons died 8, 12, and 34 hours after injury. In the remaining 11 cases the systemic embolism was less severe and there were multiple severe injuries to the head or other parts of the body making it difficult to consider the fat embolism as the direct cause of death. It is probable, however, that systemic embolism aggravates the condition of the seriously injured patient.

### Control Group

In sharp contrast to the high frequency of fat embolism in traumatic cases, very few of those in the control group had any evidence of fat in pulmonary vessels. Nine cases of natural death were examined, none had evidence of trauma, and in no case was fat embolism found. Nine cases of death by fire were also examined. These persons were of different age groups with severe burns that in some cases covered the entire surface of the body. There was evidence of aspiration of smoke and carbon monoxide but in no such case was fat embolism found.

In seven diabetics, where coma or some other complication of diabetes was the cause of death, only one showed a small amount of fat in the lung (1+). This patient was said to have had severe convulsions prior to death.

Seven poisoning cases including four due to phosphorus and three due to carbon tetrachloride were examined. Fat embolism was not found in any of them even though severe fatty degeneration and necrosis of the liver as well as fatty degenerative changes in the kidney and myocardium were present in all patients.

Sixty persons dying of chronic alcoholism were examined and 59 showed heavy fatty changes of the liver with or without cirrhosis. In only one case a slight degree of fatty embolism (1+) was found without evidence of trauma.

### Fat Embolism Following Cardiac Massage

A further series of 22 persons dead from natural causes, or from poisoning (mainly barbiturates) without evidence of trauma was examined. Resuscitation was attempted on all by artificial respiration and closed cardiac massage. In 11, slight (1+) or moderate (2+) fat embolism was found. More fat was found in those who survived for a few hours or in those with fractures of ribs or sternum.

Another series of 17 cases was examined in which an operation on soft tissue had been performed (appendectomy, cholecystectomy, deep incision, cesarean section, etc) and who died during or shortly after the operation. In only four cases a slight degree of fat embolism (1+) was found.

### Comment

There is an obvious connection between mechanical trauma and fat embolism. The most extensive and frequent appearance of fat follows injury to bone, or multiple injuries and fractures. However, injury of soft tissue such as contusion, laceration, or operation can produce embolism. In our own material we found fat embolism in 4 of 17 persons following soft tissue operations as well as in alcoholics with multiple soft tissue contusions and bruises. Bone surgery, especially nailing, produced mobilization of fat from bone marrow with subsequent fat embolization. Even shaking the bone may produce a fat embolism. The fat emboli follow trauma which mobilizes fat from bone marrow and other depots of fat in the body, especially sub-

cutaneous fat. It was frequently possible to observe during autopsy the fat (oil) accumulation around the fractured bone or lacerated subcutaneous tissue as well as in the blood effusion in the chest, abdominal cavity or hematomas. In one case of a fall from a height with multiple fractures and lacerations we saw an accumulation of about 30 ml of oil in lacerated subcutaneous tissue about the fractured sternum.

It is possible to produce fat embolism experimentally by injuring tissue such as bone marrow or by injecting oil or fat intravenously. Rechlinghausen showed that oil enters the capillaries around injured areas as well as Havers canals of bone and regional lymph nodes after injection of Zinnober suspension in oil. Increased pressure inside the injured bone or hematoma may push fat into broken vessels. This may also occur without such pressure in compound fractures or after draining the site of injury.

Another possible source of fat is the flocculation and precipitation of fat emulsion from serum. Experiments with different substances such as $\alpha$-toxin (*Chlostridium Welchii*) and adrenocorticotropic hormone (ACTH) have not successfully demonstrated this phenomenon in man. In our material there were two cases of gas gangrene. In one case, after the fracture of a leg in a 6-year-old boy who died five days later, we noted slight fat embolism which might be expected after a fracture. The other case was an 8-year-old boy with a penetrating injury of the head and gas gangrene of skull and brain who survived two days. There was no fat embolism at autopsy.

That even an excessive lipemia is unable to produce a fat embolism was demonstrated by the case of a 28-year-old male who died of acute necrotic pancreatitis. The lipemia before death was measured at 2,400 mg/100 cc. At autopsy the blood had the appearance of strawberry-colored cream but there was no evidence of fat precipitation or fat embolism. Another piece of evidence which proves that fat precipitation from blood had little significance, if any, in the production of fat embolism, is the sudden appearance of fat in large droplets and sometimes a large number of emboli immediately after the injury. The rare appearance of fat in systemic circulation is added proof. If a lipoprecipitating principle is postulated in blood after trauma, one would expect approximately the same amount of fat in systemic circulation as in the lung, but this rarely occurs.

A fatty liver is also a large depot of fat. Theoretically it is possible that liver trauma can mobilize some fat from the liver due to laceration, contusion, or concussion. We do not think that it would be possible to differentiate fat emboli from the liver from other sources of fat emboli. From our material we were not able to make any such decision although liver embolism to lung was found in one case. Durlacher and Meier have shown that in 11 chronic alcoholics with heavy fatty changes in the liver there were seven with massive fat embolism (3+ and 4+) in the lungs. In our series of 60 alcoholics we were not able to confirm this finding. Nor was it possible in diabetics with fatty changes in liver, kidney, and myocardium to find fat embolism, except for a slight degree of embolism in one case with a history of severe convulsions prior to death.

In seven cases of phosphorus or carbon tetrachloride poisoning with heavy fatty necrosis of the liver and fatty degenerative changes in the kidney and myocardium there was no fat embolism.

According to the cited evidence we can conclude that the main origin of fat is mobilized fat from fatty tissues in the body, primarily bone marrow and subcutaneous fat. The liver is not excluded as a source for fat embolism but this would occur only after mechanical trauma and not spontaneously or in connection with other changes in the liver.

The appearance of fat emboli is obviously connected with maintenance of blood circulation. It is known that after very severe injuries to the whole body or to vital organs the heart may continue to beat for a few seconds or even minutes. This is enough to transport fat to the lung and explains why embolism may be found even when a victim appears to have died immediately. Fat embolism cannot be expected when heart or big vessel laceration has occurred or after extremely severe injuries. Only a few seconds of circulation are needed to transport fat to the lung.

Disappearance of fat happens slowly. In our material we found fat emboli present in 67% of cases 15 days after injury. We do not believe that all the fat is liberated at the moment of injury. Embolism may occur in repeated attacks over a long period.

The amount of embolization depends on (1) degree and type of injury; (2) time of survival; and (3) age of subjects and quality of medical care. Even in very severe injuries massive fat embolism would not be expected if the patient died quickly. The most pronounced embolization is

seen in persons dying between 6 and 24 hours after injury. The age of the patients has an influence on the amount of fat. An older person (50 to 80 years) is prone to show more embolization than a younger one probably due to the larger amount of fatty tissue and the consistency of his fat. Immediate immobilization of fractures and careful transportation of an injured person will greatly reduce the risk of fat embolization.

By manipulation it is evidently possible to precipitate fat embolization. We were able to show fat embolism in lungs in persons who died of natural causes without previous trauma but on whom closed chest cardiac massage had been performed. The amount of fat was never very large (1+ and 2+), and embolism was found more frequently in persons who survived for a few hours or in persons who sustained fractures during the massage. It can be questioned whether the patients with fat embolism who did not survive the massage were not still alive during the procedure. It is possible that a certain amount of blood can be passively pushed to the lung by cardiac massage but it is questionable if blood with droplets of fat could passively enter the heart from the injured tissue (fractured ribs). It is likely that these persons who seemed to be dead probably had some heart action during the resuscitation.

Embolism of bone marrow has the same significance as fat embolism but means that some bone has been injured. We have not seen bone marrow emboli without bone injury but violent shaking of bones without a fracture could possibly cause a bone marrow embolism. The particles of bone marrow are usually larger than fat droplets so there is little possibility of their penetrating the systemic circulation.

The appearance of fat in systemic circulation always follows a massive lung embolism. In our material the foramen ovale was always closed indicating that the fat passed the capillary barrier of the lungs. In two deaths after a helicopter crash we found a few fat emboli in the brain in one case, and some big droplets of fat in a renal arteriole in the second case. Both of the victims of this crash were found dead at the scene. According to these findings it seems possible that fat can penetrate the systemic circulation very rapidly, perhaps a few seconds after entering the lung. In three of the remaining cases, the systemic embolism was found one-half and two hours after the accident.

Fat embolism of the lung does not seem to be dangerous to health. Of course it is possible to produce death experimentally with large amounts of fat but in man it is not probable that such large amounts of fat are ever mobilized. On the other hand, massive lung embolization can easily aggravate the condition of an injured patient. In contrast, systemic embolism is always a serious event because of damage to the brain circulation, and it may be the main, or a contributory cause of death.

## Conclusion

Fat embolism follows mechanical trauma which mobilizes the fat from an injured fat depot in the body. This happens rapidly, usually within a few seconds after injury and a few heart beats are sufficient to bring fat to the lungs and even to the systemic circulation. For this reason fat may be found even when death seems to be instantaneous although with sudden death the amount of fat is usually small. The amount of fat in those surviving injury is proportional to the degree of injury and to the time of survival up to 24 hours. Older persons are prone to have more massive fat embolization.

Systemic embolization can appear almost as rapidly as pulmonary embolism and enters the systemic circulation through the lung capillaries. They are more frequently seen in the kidney than in the brain. The clinical symptoms and later fate of the patient depend on the amount of fat mobilized. The finding of petechial hemorrhages in the skin, conjunctiva, mucous membranes, and fundus of the eye, as well as the finding of fat droplets in sputum, urine, or blood can help make a diagnosis of systemic embolism during life.

Pulmonary fat embolism is rarely found without trauma. In such cases the amount of fat is very small and never appears in the systemic circulation. Closed chest cardiac massage can result in a small amount of fat embolism depending upon the extent of the injury produced as well as the duration of the survival.

Although pulmonary fat embolization apparently has little effect on the survival of most injured patients, systemic fat embolization is a serious event with a high mortality (38%). Since no effective therapy has been developed for this condition prevention by careful movement of the accident victim is of great importance.

(The figures and references may be seen in the original article.)

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# UNEXPLAINED SYSTEMIC MANIFESTATIONS OF MALIGNANT LUNG TUMORS

*DeWitt C. Daughtry MD, FCCP,* John G. Chesney MD,***
*Harold C. Spear MD, FCCP,† Thomas O. Gentsch MD, FCCP,††*
*and Parry B. Larsen MD, Miami, Florida, Dis Chest 52(5):*
*632–639, November 1967.*

During the authors' experience in the diagnosis and management of over 1,600 primary lung tumors in private practice, many rare cell types, multiple cell types in the same tumor, multiple tumors in the same patient, unusual metastases, and many unusual local and systemic manifestations have been encountered. The most fascinating features have been the unusual physiologic manifestations, at least some of which seem to be the result of the production of hormones by the tumor or stimulation of the endocrine glands by the tumor to secrete abnormal amounts of hormones. The mechanism is not clear. One might just say that these fascinating physiologic aberrations are due to the tumor-host reaction. These reactions may be as variable or bizarre as are the people who harbor and nourish these pulmonary tumors. An attempt will be made to discuss the clinical features of the various syndromes, to present typical illustrations and, to some extent, theorize on their etiology.

### *Hypertrophic Pulmonary Osteoarthropathy*

The presence of clubbing of the fingers and toes and mild to severe osteoarthralgia and/or hypertrophic osteoarthropathy have attracted attention for several decades. It occurs in approximately 10 percent of malignant lung tumors. The extent of clubbing varies greatly and ranges from curved nails to marked enlargement of the distal one-half of the terminal phalanges. The volar pads may become very thick and firm and the skin immediately adjacent to the nails may develop a violaceous-red color. The joints may be enlarged, painful, warm and occasionally hyperemic. X-ray examination of the involved areas may be negative or show considerable periosteal proliferation of the shaft of the long bone. Occasionally, new bone may be deposited in the terminal phalanges and in the long bones. These somewhat different manifestations are usually lumped together and called hypertropic pulmonary osteoarthropathy. No general explanation or theory has been widely accepted as to the pathologic physiology involved. Its occurrence is unrelated to malignant cell type except that it is found in nearly 50 percent of patients with mesothelioma of the pleura. It is uncommon in women with carcinoma of the lung. Interestingly enough, the severe pain, swelling and periosteal reaction do not, as a rule, respond to local or systemic therapy including the corticosteroids. One of the most interesting features is the dramatic disappearance of all symptoms within a few minutes after the patient reacts from the anesthetic when the primary tumor has been resected. This may occur even when the primary tumor has been resected, but extensive metastases remain unresected. The clubbing and periosteal reaction of digits recede more slowly and less completely.

Hypertrophic osteoarthropathy seen in lung tumors may be mild and consist clinically of only mild stiffness and aching in the joints with or without clubbing or they may be severe enough to incapacitate the patient. Sometimes the pain and soreness is so extreme that the patient cannot be turned in bed without great discomfort. This manifestation may precede clinical discovery of the tumor by several years. Carcinoma of the lung should be suspected with the onset of each new case of "arthritis" or the appearance of clubbing and appropriate studies performed. Of course, several other conditions such as bronchiectasis, arteriovenous fistula of the lung, chronic lung abscesses, severe pulmonary fibrosis, mucoviscidosis, chronic empyema, ulcerative colitis, cirrhosis of the liver, and other less common disorders may produce hypertrophic osteoarthropathy. Rarely one encounters familial clubbing of the fingers.

*Clinical Associate Professor of Surgery, University of Miami School of Medicine; Chairman, Department of Surgery, Miami Heart Institute.
**Clinical Assistant Professor of Surgery, University of Miami School of Medicine.
†Clinical Assistant Professor of Surgery, University of Miami School of Medicine.
††Clinical Associate Professor of Surgery, University of Miami School of Medicine.

*Neuromyopathy*

Neuromyopathy, in varying degrees, may be associated with 15 percent of malignant tumors of the lung. Mild to moderate weakness is common, but the severe form of prostrating neuromyopathy is rather rare and may be so profound as to divert the clinician's attention away from the possibility of a malignant tumor of the lung. The severity of this condition is not in proportion to the size of the tumor. It is most often associated with the small cell type, often called "oat cell" carcinoma of the lung. The neuromyopathy syndrome being considered is not a result of metastases to the central nervous system.

There is proximal weakness of the limbs, usually the lower extremities, and is associated with diminished reflexes. It is not a part of a state of general cachexia, for we have seen it occur suddenly in rather robust, strong individuals without any evidence of weight loss or anything else to point toward a lung tumor. In some cases, it is quite similar to amyotrophic lateral sclerosis. It occurs most often in men and may become manifest several years prior to the development of clinical cancer. Motor neuro degeneration may occur and removal of the tumor may not reverse the nervous system changes.

Case Report

A fascinating case of a 62-year-old physician may elucidate the condition better than a general discussion. This active surgeon felt some weakness in his legs for two or three days, but had been going about his work until he arose one morning to find that he could not stand because of profound muscle weakness. Within a few days, his arms became so weak that he could not feed himself and this condition became so generalized that it involved the muscles of deglutition and respiration. It was necessary to introduce a feeding tube and to perform a tracheostomy. His speech was slurred and it was difficult for him to express himself.

He gained about 40 pounds in weight, but finally died due to weakness of the accessory muscles of respiration and pulmonary suppuration secondary to the aspiration of nasal and oral contents. At necropsy, nothing was found wrong with the nervous system but a small previously undisclosed "oat cell" type of carcinoma was discovered in the left lower lobe of the lung. No metastasis was detected. The lesion had not been detected on serial x-ray studies taken because of cough and pulmonary suppuration. This patient had been treated on the neurologic service where diagnosis of obscure neuromyopathy had been made.

*Malignant Carcinoid Syndrome*

Malignant carcinoid syndrome secondary to a carcinoid type of bronchial adenoma remains a rare but very fascinating lesion. This syndrome is due to a release of a large amount of serotonin into the blood stream, producing transient and recurring flushing of the upper half of the body, fluctuation in the blood pressure, abdominal cramps, vomiting, diarrhea, tachycardia and often severe electrolyte imbalance. Sudden shock-like death may occur. Often wheezing, dyspnea, hyperpnea, tricuspid valve insufficiency and pulmonary valve thickening and stenosis occur. The latter two may produce right heart failure. In the absence of liver metastasis, the hepatic circulation is bypassed and left-sided heart valve lesions may occur. The serotonin is transformed into 5-hydroxylindoleacetic acid which is excreted in the urine in abnormal amounts if liver metastasis occurs. Serotonin is formed from tryptophane, an amino acid. Normally, only a small percentage of tryptophane is converted into serotonin but in malignant carcinoid syndrome, 50 percent or more of the tryptophane is converted, by the body, to serotonin.

The symptoms and findings may be intermittent and the diagnosis is difficult to establish except during the exacerbations when the urinary output of 5-hydroxylindoleacetic acid may rise from the normal of nine up to as much as 600 mg per 24 hours. This establishes the diagnosis. It appears that liver metastasis is necessary for the production of hyperserotoninism or the malignant carcinoid syndrome. The process is usually fatal, but may follow a very slow and intermittent course for several years because of the low grade nature of the malignancy. Serotonin may be found in the tumor by chromotography and by bioassay.

The diagnosis is simple once it has been considered. Pathology report may be that of adenocarcinoma of the lung, but certainly the clinical course is not that of the usual adenocarcinoma. The attack may be precipitated by drinking beer or other alcoholic beverage and by emotional stimulation. Dehydration, hypoproteinemia, vitamin B deficiency, fever and electrolyte imbalance often result. The liver is usually enlarged due to metas-

tases and it occasionally pulsates. Complete or subtotal removal of the tumor usually brings relief. If the tumor is not resectable, palliation may be accomplished by the administration of a high protein diet, vitamin B, maintenance of hydration and the use of atropine-like drugs. Occasionally, cardiac failure requires treatment.

Case Report

We encountered a very interesting example of malignant carcinoid syndrome in a 51-year-old nurse. Hemoptysis was her only early symptom. Her very small right lower lobe tumor was resected elsewhere and was called "adenocarcinoma of the lung." Two years later she developed intermittent flushing of the trunk, neck and face, abdominal cramps, diarrhea and extreme weakness. Three to four years later, she developed a large liver and the abdomen was explored. The biopsy from the liver yielded a diagnosis of "metastatic adenocarcinoma, probably from the lung." No source of metastatic carcinoma was found in the abdomen. She had the typical clinical picture of malignant carcinoid syndrome, but the diagnosis had not been made during evaluation in two other major medical centers. After several negative studies of the urine, a highly positive 5-hydroxylindoleacetic acid level was found during a severe exacerbation of her symptoms. She did moderately well over a period of seven or eight years with only a moderate weight loss. She suddenly succumbed within a period of 24 hours from severe dehydration and electrolyte imbalance secondary to violent vomiting and diarrhea which occurred while she was vacationing in a small resort town.

Masculinizing Syndrome

This rare syndrome occurred once in the author's experience and it can best be depicted by reporting the case in some detail.

Case Report

A 36-year-old white woman, mother of three children, had not menstruated for six years. During these six years, she had developed masculine features of rough skin, acne, male hair distribution, atrophy of her breasts, enlargement of the clitoris, a husky voice and a growth of facial hair that necessitated shaving two or three times a week.

Pelvic examination was negative and the endocrine studies performed failed to reveal any abnormality. This was, however, some 15 years ago when endocrine studies were not highly refined. She had been aware of a tumor in the right lower lobe of the lung for approximately six years and she had been experiencing intermittent hemoptysis.

She was informed that removal of the tumor should be performed, but that she should not expect disappearance of the masculine features. The tumor was removed and found to be a carcinoid variety of bronchial adenoma. Over a period of a few months, there was moderate recession of her masculine features. It was no longer necessary for her to shave. Pregnancy occurred within six months. She has remained well during the past 15 years and has continued to menstruate.

*Hypoglycemia*

Severe hypoglycemia is a rare complication of carcinoma of the lung and may occasionally result from a large benign intrathoracic fibroma or mesothelioma of the pleura. Hypoglycemia does not occur, as a rule, until the tumor mass reaches a large size. The mechanism of production of this syndrome is unknown, but excessive glucose utilization by the tumor could explain the alteration.

We have encountered, on a number of occasions, mild degrees of hypoglycemia, but only once have we encountered a severe degree of hypoglycemia associated with carcinoma of the lung.

Case Report

A 50-year-old colored man, smoker, with severe osteoarthropathy was admitted to the hospital in a very weak, almost comatose state one year after having been discharged from the same hospital with "a pneumonia which did not completely clear." This patient's blood sugar would intermittently drop from 50 to 25 mg percent and on one occasion to as low as 10 percent. The patient's severe hypoglycemic symptoms could not be relieved until 25 to 50 percent glucose was administered intravenously. This syndrome was relieved by resection of an epidermoid carcinoma of the left lung. Metastases remained in the mediastinum, but he had no further recurrence of the hypoglycemic state during the several additional months which he lived.

At necropsy, the pancreas was found to be normal and the endocrinologist who evaluated this patient thought the tumor secreted an insulin-like substance or some substance which stimulated the pancreas to secrete an excessive amount of insulin.

*Hypercalcemia*

Severe hypercalcemia is indeed a rare complication in carcinoma of the lung and is found in a few other tumors not involving the parathyroid glands or bones. Anderson and Glenn reported hypercalcemia in 20 patients with neoplasms not involving the parathyroids or the bones. One of these was in a patient with squamous cell carcinoma of the penis. The serum calcium level, in this patient, reverted to normal within 24 hours after excision of the tumor. Again, it is difficult to state whether or not these tumors elaborate the parathyroid-like hormone or some substance which in turn stimulates the parathyroids to excrete an excessive amount of parathyroid hormone. The parathyroid glands may show hypertrophy and the process can be reversed by subtotal resection of the parathyroids if the malignant tumor is unresectable. Of course, removal of the malignant tumor is the ideal treatment and reverses the process promptly. Mild hypercalcemia, which occurs in some of the carcinomas of the lung, can be explained on the basis of bony metastases. Abnormal vitamin D metabolism and/or increased absorption of calcium in the intestinal tract may be possible explanations.

Case Report

We had the occasion to see a 55-year-old colored man who was hospitalized because of severe weakness, weight loss and restlessness of several weeks' duration. He was a heavy smoker and had a cough for several weeks. X-ray revealed a 12 cm discrete tumor mass in the right lower lobe of the lung. Over a period of a few days, a small cavity appeared within the tumor. um calcium determinations ranged from 18 to 23 mg percent and phosphorus was 2 mg percent. He died while investigation was underway and while he was being prepared for surgery. Necropsy was refused, but previously a needle biopsy had been performed and a pathologic diagnosis of epidermoid carcinoma of the lung was made. There was no evidence of metastatic disease.

*Cushing-like Syndrome*

A syndrome closely resembling Cushing's syndrome may occur in patients with small cell or so-called "oat cell" carcinoma of the lung. Common features seen in this syndrome of adrenal cortical hyperplasia and hypersecretion associated with carcinoma of the lung are chiefly those of marked laboratory aberrations seen in Cushing's syndrome, but often without the classic physical features. Patients have a somewhat round and plethoric face and occasionally brownish stippling of the skin, but often the physical signs are absent. The electrolyte changes are more profound than in Cushing's syndrome and these patients often lose weight rapidly and develop progressive weakness. Obesity may not develop because of the short duration of the carcinoma. Marked hypokalemia, hyponatremia and metabolic alkalosis are common features. Hypertension, mild diabetes and glycosuria are inconstant while polydypsia, polyuria and mental confusion are common. Death is hastened by the complication of adrenocortical hyperfunction such as hypokalemia, cardiac failure and sepsis. This syndrome may precede the clinical appearance of the tumor.

Hypertension is seen in 50 percent of the patients and may in part be due to sodium reabsorption and retention. The potassium secretion is increased probably because of the increased sodium reabsorption at the expense of the hydrogen ion despite the cellular potassium deficit. The continuous loss of cellular potassium produces intracellular shift of sodium and hydrogen ion which allows the serum bicarbonate to rise and a resulting alkalosis. Estridge, Hughes and Hammond found the 17 ketosteroids and 17 hydroxycorticoids to be elevated in all but one case tested. They reviewed 38 previous cases and added five new cases. They found the plasma hydrocortisone levels to be high in all cases tested and the aldosterone levels to be normal.

Biologically and physiologically, the tumors contain adrenocorticotropin or corticotropin-like substance indistinguishable from pituitary corticotropin. Bioassays of the tissue of the pituitary gland have shown decreased ACTH content indicating suppression of function by the increased levels of circulating hydrocortisone. The metastatic lesions also contain corticotropin-like substance. Necropsy often reveals adrenal cortical hyperplasia and quite often liver metastases.

The condition may, upon superficial evaluation, appear to be cardiac failure. Management requires preoperative attention to the correction as well as the possibility of the electrolyte disturbance by the administration of potassium, limitation of fluid and salt intake and the use of antibiotics. Surgical removal of the malignancy reverses the process if

no metastasis remains. If the tumor cannot be removed or if metastases remain, electrolyte abnormalities are difficult or impossible to correct. Partial or total adrenalectomy should be considered in those cases in which all of the tumor is not resectable and when the patient's condition will not permit pulmonary resection. The temporary remission obtained thereby is, of course, of short duration.

*Feminizing Syndrome*

Gynecomastia is one of the more common systemic manifestations of carcinoma of the lung, usually in the adenocarcinoma type. Gynecomastia may be mild or marked and usually clears upon resection of the tumor. It also reappears if the tumor recurs. The patient's voice may become high pitched and the testicles may atrophy. The level of circulating estrogen may be appreciably elevated, but reverts to normal and there is at least partial reversion of the other findings upon resection of the tumor. The breasts show considerable proliferation of the ductal system.

Case Report

The following case will illustrate most of the classic manifestations of this syndrome. This white man, 62 years of age, was admitted with chest pain, cough, weight loss, high pitched voice and obvious gynecomastia. The tumor-containing right upper lobe was resected. The size of the breast decreased appreciably, but gynecomastia recurred one year later coincident with the recurrence of obvious clinical metastatic carcinoma. The pathologists reported both squamous and adenocarcinoma cell types in the resected tumor.

The explanation of this gynecomastia in carcinoma of the lung is unknown. The adrenals may be stimulated to secrete estrogen as occasionally seen in male adolescents. Some interference with testicular function may produce the aberration. Alterations in liver physiology may be a factor in the production of this syndrome.

*Miscellaneous Groups*

Additional systemic manifestations of carcinoma of the lung include the acetylcholine-like substance and the oxytocic activity in hemangiopericytoma, systemic sclerosis, the hyponatremia syndrome. McCormick and co-workers of the Cleveland Clinic and Andersen *et al* have presented a number of very interesting "functioning" pulmonary neoplasms associated with excessive secretion of antidiuretic hormone, myasthenia gravis-like syndrome, dermatomyositis associated with marked muscle weakness, brawny edema and erythema of the skin, cerebellar degeneration of the Purkinje cells producing vertigo, ataxia, dysarthria, diplopia, but with preservation of the intellect. They have further presented extrapulmonary manifestations of bronchogenic carcinoma such as acanthosis nigricans, scleroderma, peripheral neuropathy, mental changes and toxic psychoses.

Hematologic changes are occasionally observed, some of which are polycythemia, hemolytic anemia, hypochromic anemia, generalized malaise and anorexia, purpura and thrombocytopenia. Lung tumors are commonly accompanied by thrombophlebitis, phlebothrombosis and pulmonary embolism.

Early in the clinical stage of carcinoma of the lung, an occasional patient reports increased appetite, weight gain and a sense of well being not previously experienced during recent years. We offer no explanation for this type of reaction.

Summary

Pulmonary tumors may be bizarre and variable in their clinical manifestations. The authors and others have recently focused attention upon systemic effects of malignant tumors, some of which seem to be the result of the production of hormones by the tumor or stimulation by the endocrine glands by the tumor or a product of it, to secrete abnormal amounts of hormones. The mechanism is not clear. This again may be just another abnormal host reaction to the tumor. The physiologic aberrations are interesting and, as a rule, the prognosis in these "hormone-secreting" tumors is rather unfavorable.

In the authors' personal series of over 1,600 lung tumors, several patients with severe hypertrophy, and pulmonary osteoarthropathy, have experienced immediate relief after the removal of the tumor even though metastases remained unresected. The unusual and fascinating neuromyopathy, malignant carcinoid syndrome, masculinizing syndrome, marked hypoglycemia, Cushing-like syndrome, feminizing syndrome, and other systemic manifestations have been encountered in the management of malignant lung tumors. An intensive study of these fascinating and uexplained physio-

logic manifestations should shed important light on these, and possibly many other physiologic aberrations.

The various systemic manifestations of malignant lung tumors have been discussed and illustrative cases presented.

(The omitted figures and references may be seen in the original article.)

# MEDICAL ABSTRACTS

## PULMONARY GRANULOMATOSES DUE TO INHALED ORGANIC ANTIGENS

*John Rankin, MD, Mosaburo Kobayashi, MD, Robert A. Barbee, MD, Helen A. Dickie, MD, Med Clin N Amer 51(2):459–482, March 1967.*

Inhalation of a wide variety of organic dusts by individuals sensitive to antigens present in the dusts may result in acute, chronic, or recurrent lung disease with symptoms and signs attributable to a reaction in the most peripheral part of the bronchopulmonary tree. High titers of precipitating antibody against antigens present in the dusts are found in the sera of affected individuals. The most striking tissue reactions consist of diffuse infiltration of the interstitial tissues of the lung with plasma cells and lymphocytes, epithelioid cells, poorly defined tubercles, and Langhan's giant cells.

The various diseases known as farmer's lung, thresher's lung, bagassosis, mushroom worker's disease, maple bark disease, bird breeder's (fancier's) lung and probably several other conditions are merely different clinical expressions of the same basic immunopathologic mechanism. The antigens capable of producing this type of reaction are ubiquitous, and are likely to be a fairly common cause of lung disease. In most instances, diagnosis can be established by the judicious combination of clinical, radiologic, physiologic, serologic, and histologic techniques.

## CARCINOMA OF THE PROSTATE: TREATMENT COMPARISONS

*The Veterans Administration Cooperative Urological Research Group, J Urol 98(4):516–522, October 1967.*

In this series the average patient with prostatic carcinoma did not derive much clinical benefit from immediate treatment with either orchiectomy or a 5 mg. daily oral dose of stilbestrol unless the cancer was causing serious problems. The excess mortality associated with estrogen therapy, the psychological trauma of orchiectomy, the adverse effects of the placebo itself and the clinical benefits obtained when patients with progressing disease were shifted from placebo to more active treatment, all combined to suggest therapy by estrogen or orchiectomy should be withheld until the patient's symptoms are so severe as to require relief. Treatment earlier in the disease is not likely to help and may cause considerable damage. Either estrogen alone or orchiectomy alone provided all the clinical benefits of the two in combination.

## TISSUE ADHESIVES IN FATAL HEMORRHAGE FROM SOLID ORGANS

*LTC Teruo Matsumoto, MC, USA, Milit Med 132(12):951–962, Dec 1967.*

Surgical techniques have been developed for hemostasis of solid organs, using higher homologous cyanoacrylate monomers.

N-butyl, isobutyl and the monomer mixture of 95% heptyl-5% methyl cyanoacrylate monomer may be used clinically only in an emergency situation as a life-saving procedure.

At present the best monomers are n-butyl, isobutyl, and a monomer mixture of 95% heptyl-5% methyl cyanoacrylate.

A sterile, individually disposable spray unit for aerosol tissue adhesive spray has been developed which is simple and effective for surgical application of tissue adhesive.

## TREATMENT OF TATTOOS

*B. N. Bailey, FRCS, Plast Reconstr Surg 40(4):361–371, Oct 1967.*

The main indications for removal of tattoos in prison population are mentioned.

The techniques available for tattoo removal are considered, and the method of shaving, punctate excision and skin grafting is described in detail.

Complications are described and the natural history of grafted areas briefly considered.

### STUDIES OF VENEREAL DISEASE II. OBSERVATIONS ON THE INCIDENCE, ETIOLOGY, AND TREATMENT OF THE POSTGONOCOCCAL URETHRITIS SYNDROME

*LT King K. Holmes, MC, USNR; LCDR David W. Johnson, MC, USN; CAPT Thomas M. Floyd, MSC, USN; and LT Paul A. Kvale, MC, USNR, JAMA 202(6):474–476, Nov 6, 1967.*

Postgonococcal urethritis (PGU) occurred in nearly two thirds of men with gonorrhea acquired in the Far East who were "successfully" treated with 2,400,000 units of procaine penicillin G plus probenecid. PGU occurred less often after treatment of gonorrhea with tetracycline hydrochloride, and PGU itself responded to tetracycline, suggesting a microbial etiology for the condition. The syndrome was associated to a highly significant degree with *Mycoplasma* infection of the urethra, and occurred more often after infection with *Neisseria gonorrhoeae* of lessened penicillin sensitivity. The high incidence of the syndrome, one of the most common infectious diseases among military personnel in the Far East, requires a reexamination of the traditional use of penicillin in the treatment of gonorrhea in men.

### DEEP-SEATED MYCOTIC INFECTIONS, ALLERGY TO FUNGI AND MYCOTOXINS

*Donald B. Louria, MD, New Eng J Med 277(20):1065–1071, Nov 16, 1967.*

Interest has increased markedly during the last decade in systemic fungous infections as well as in 2 disparate but related areas, pulmonary allergy to fungi and the extraordinary effects of mycotoxins. This article reviews some of the more interesting data concerning the pathogenesis, clinical manifestations and immunology of these sometimes life-threatening diseases. No attempt is made to be comprehensive but instead there is concentration on the studies published for the most part during the last ten years that appear to be of greatest significance. Higher bacteria such as *Actinomyces israeli* and *Nocardia asteroides* are included.

# DENTAL SECTION

### INNOVATION IN DENTISTRY

*RADM F. M. Kyes, DC USN, Assistant Chief for Dentistry and Chief, Dental Division, Bureau of Medicine and Surgery.*

Two recent books dealing with changing technology point up the Dental Corps' problems in the area of innovation which is defined as "the practical application of new technology." *Technology and Change*[1] by Donald Shon and *Uncertainty in Research Management, and New Product Development*[2] by Raymond Hainer, Sherman Kingsbury and David Gliecher, support this concept.

The induction, encouragement and channeling of innovation are difficult in industry because money is involved. Innovation is accepted in dentistry with even less enthusiasm because health is involved. Many dental officers resist change because they are satisfied with and accept the status quo, and do not wish to take on something the results of which they cannot completely and rationally predict.

In a corporation the President, as a "product champion," may order a program and sell it throughout the organization. In the Dental Corps, where the dental officer makes the ultimate decision regarding treatment for each patient, the innovation process is immensely more difficult.

Advances have been interpreted as orderly progress from invention to utilization, but the authors take a different view and point out that eventual usage is non-rational and is a slow process of development. This has surely been true in the stannous fluoride program. When the first studies were commenced at New London, few foresaw group therapy, self-preparation, trailers, the children's program, large numbers of additional hygienists,

1. New York Delacort Press, 1967.
2. Reinholt Publishing Corp., New York, 1967.

or other facets of the final monument as it was eventually cut.

The premise of both of the above books is that organizations resist change. Actually, the stannous fluoride program was an addition rather than a technical change. Its acceptance by the organization was faster than might have been expected. Similarly, after a preventive program in periodontics is developed and tested in pilot studies, its acceptance will probably be as speedy as personnel capabilities will permit because it is an addition and not a change.

The third area, tooth conservation, in the Dental Corps is somewhat different and gets into the major problem areas described by the authors in corporation management. The broad use of temporary restorations in times of peak loading, deployments, etc., is not an addition but a "change." To most dental officers it is a threat. Leaving decay under a restoration in an indirect pulp capping may reflect unfavorably on their professional reputations. Using cement alloy, which might eventually be considered by civilian dentists as a "poor amalgam," is a threat to the Navy's dental treatment reputation. The Dental Corps' top management has mildly pushed the idea of wider use of temporary restorations (during peak loads) for tooth conservation for the past seven years, but there has been no "product champion" pushing it throughout the Corps. Schon's and Hainer's texts indicate why innovation has not taken place in this third large area of potential improvement. A reviewer of the two books in the Industrial Bulletin states, "For the risks of innovation to be taken, management must itself come to be strongly involved in the innovative process, or it must become possible for a 'product champion' to fight his innovation through the whole system. These are two 'models for change' that are suggested as necessary new approaches to organizations for innovation."

If you ask any dental officer, "Would you rather have your son go to Vietnam with five open cavities and two highly polished amalgams or with seven temporary restorations of known and acceptable longevity?", he will take the latter for his own son every time. For someone else's son, the threat of "sloppy dentistry", censure by civilian dentists, and pride of workmanship coupled with the myth that one can put in an amalgam as fast as a cement restoration, all serve to default a program which should have been accepted long ago.

In February, 1968, color coded temporary restorations will become available. With a red restoration to indicate underlying caries and a green restoration to indicate all caries removed, possibly this third area of tooth conservation will become as palatable as caries and periodontic prevention. If and when this happens, it will have to be remembered that senior dental officers are "management" and will also have to be "product champions." Once the "threats of change" have been removed by color coded temporary restorations, possibly this third opportunity for tooth conservation may be capitalized.

## CURRENT BASIS FOR PREVENTION OF PERIODONTAL DISEASE

*J. Waerhaug, Int Dent J 17:267, June 1967.*

Before periodontology was recognized as a separate and distinct discipline, it was taught under the guidance of various dental specialties. As a result, the treatment of periodontal disease was developed on a purely empirical basis. A variety of treatment procedures was introduced depending on the philosophy of the department in which the subject was taught.

Through the efforts of epidemiologic surveys and clinical trials, many of the traditional therapeutic methods have been shown to be without a rational basis and the justification for others has been seriously questioned. However, of equal importance, these surveys and studies have convincingly substantiated the role of other etiologic factors and the efficacy of some treatment methods has become evident.

On the basis of the most recent clinical and experimental studies, periodontitis may be classified as a bacterial disease. Since we are now aware of this etiologic factor, it becomes quite obvious that preventive measures must be directed against the causative agent, the bacterial plaque. This may best be accomplished by removing the plaque so frequently and so efficiently that the bacteria will be unable to launch their destructive forces.

The prevention of periodontal disease is, therefore, dependent on the cooperation of the patient and dentist in removing the plaque from the teeth and in maintaining a clean environment. In the prevention of periodontal disease, patient motivation is the key to success. This requires the patients not only to be informed about the cause and consequence of periodontal disease, but also

to be thoroughly aware of the beneficial effect of meticulous home care.

The role of the dentist in the prevention of periodontal disease must not only be to motivate and instruct, but also to diligently remove plaque from inaccessible areas during a prophylaxis. Care should be taken by the dentist so that he does not become directly involved in the etiology of periodontal disease by the placement of unsatisfactory restorations.

(Abstracted by: CDR Joseph J. Lawrence, DC USN.)

## PERSONNEL AND PROFESSIONAL NOTES

### DENTAL HEALTH STATUS OF 1,000 NAVAL PERSONNEL UPON RELEASE FROM ACTIVE SERVICE

A group of 1,000 naval personnel recently being processed for release from active service at the Naval Station, Treasure Island, San Francisco, California, were given a Type III examination. The Type III examination was conducted utilizing mouth mirror and illumination with only the occasional use of a dental explorer. A breakdown as to classifications by numbers and percentage is as follows:

| *Class* | *Number* | *Percentage* |
|---|---|---|
| I | 605 | 60.5 |
| II | 238 | 23.8 |
| III | 107 | 10.7 |
| IV | 45 | 4.5 |
| V | 5 | .5 |

This generalization can be made: Most of the 1,000 patients examined in this group were found to have cleaner mouths upon discharge than they presented upon enlistment. The overwhelming majority had received considerable dental care at naval facilities while on active duty. Specifically, the following observations are evident:

1. Personnel leaving the naval service in dental classification II were found to have 1.78 caries per man.

2. Those in Class III had 4.22 carious surfaces per man.

3. Some of the patients in Class II and Class III could also qualify for Class IV.

4. A significant few of the Class III patients could also be considered in Class V. The few men in this category either refused to admit to dental pain or for other reasons did not seek available dental treatment.

5. The Class IV grouping was considered reasonably small in number. Many of these patients had been provided with dental prostheses by the naval establishment but for a number of the usual reasons, were not wearing the appliances upon examination. An occasional patient in this class indicated that he did not receive dental prosthetic care because he either was unable to make himself available for it, or the service was unavailable at a convenient time.

6. Others in Class IV—awaiting imminent discharge from the naval service did not want dental prosthetic treatment if such care involved any delay whatsoever from the discharge processing.

### PROCUREMENT OF ULTRASONIC PROPHYLAXIS UNIT

It has been brought to the attention of the Dental Division that there appears to be some misunderstanding concerning the procurement of the *Ultrasonic Prophylaxis Unit*, FSN 6520–890–1584, and its inserts.

This unit is a Status Code II item and, as such, is a local purchase item. This does not mean that the consumer cannot procure directly from the manufacturer. The manufacturer has a GSA Contract (GS–00S–72734) and by dealing directly a 25% savings can be realized.

The inserts for this unit are Status Code I items and are to be requisitioned from the Federal Supply Catalog. The six standardized inserts are illustrated in the Catalog. However, for further clarification the following chart identifies the item as described in the Federal Stock Catalog:

| *Federal Stock Catalog* | *Manufacturer's Catalog* |
|---|---|
| Curette | Curettage P–10 Insert |
| Flat-Hoe Chisel | Hoe Type P–3 Insert |
| Left Hatchet | Hatchet Type Left P–4–L Insert |

| *Federal Stock Catalog* | *Manufacturer's Catalog* |
|---|---|
| Right Hatchet | Hatchet Type Right P–4–R Insert |
| Small Universal Scaler | Small Universal Scaler P–7 Insert |
| Straight Scaler | Straight Scaler P–1 Insert |

These inserts may be autoclaved, however, in time the "O" rings will deteriorate. "O" rings are listed in the GSA Contract and can be replaced at a local level.

### CONVERSION OF HANAU FACE BOW

Present Hanau Face Bows as supplied by the Hanau Manufacturing Company, Incorporated, 80 Sonwill Drive, Buffalo, New York 14225, to FSN 6520–501–0060 may be converted to provide a vertical landmark transfer (infra-orbital notch) by adding (1) clamp 132–101 and (1) orbital pointer 132–3015. The clamp may be added by driving out the pin which attaches the frame to the bow and removing frame by twisting off the bow. The clamp is then placed over the bow and the frame replaced with the pin hole aligned with the bow portion, replacing pin by driving in. Prices of these parts, f.o.b., Buffalo, New York are:

| | | |
|---|---|---|
| (1) Clamp 132–101 | @ | $3.33 each |
| (1) Orbital Pointer 132–3015 | @ | $ .97 each |
| (1) Clamp Wrench 132–102 | @ | $ .93 each |

# NURSE CORPS SECTION

### INTERNATIONAL WARD ON THE USS REPOSE

*LT Frances McKown, NC USN and*
*LT Annelle Lee, NC USNR.*

Since her recommissioning, the USS REPOSE has been providing medical care for our fighting men in Vietnam. Along with this primary purpose, she has been actively engaged in the People to People program—utilizing our knowledge and facilities to assist the Vietnamese with their health problems.

We do not go into the villages, as this would be very difficult from a ship-based facility, so our patients are referred to us. This referral originates with a civilian or military hospital and, often, with our own field medical-aid stations. For this reason, our teaching and care is on an individual basis and though we hope that things taught by us will be passed on to others, we cannot engage in community health teaching.

Our patients come to us with a large variety of conditions. Some have been injured in the conflict and require treatment. For the most part, however, the patients sent to us are those with congenital defects or disease-produced defects requiring corrective surgery using the advanced techniques and equipment available on the ship.

Life on our eighteen bed International Ward is very different from that to which these people are accustomed. Everyday they are confronted with the new, strange and, often, incomprehensible ways of twentieth century America, and this only a few miles from the fishing and farming villages of their homeland. To keep the experience from being too overwhelming or traumatic, our staff of doctors, nurses, corpsmen and interpreters work together to provide an atmosphere of understanding, tolerance and acceptance. This is done through study of the Vietnamese culture, a gentle introduction of the new, loving kindness, and a great deal of patience that does not give up when one step forward results in three backwards, as so often happens.

Along with medical tests and treatments necesitated by the patient's condition, health teaching has been one of the nurse's primary responsibilities. This must start with the most basic concepts, which we all take for granted, such as spitting on the floor, dental hygiene, and bathing with soap. Of course this involves teaching them the use of such unfamiliar objects as the toothbrush, a shower (scared at first, they soon learn to love it) and a commode. The age difference of our patients sometimes complicates the teaching since, at any given time, we may have a range from six years to fifty years of age. Once the patients understand what is expected, however, they are of great help in instructing and caring for the younger.

The Vietnamese adapt readily to American foods, with a few variations. Rice is served with their meals, instead of potatoes, and they season

their meats generously with "unkum", a fermented fish sauce popular in Vietnam. Other than this, they show a preference for apples, oranges, breakfast rolls and "cokes" over our favorites of pie, cake and ice cream. After surgery, or when very ill, warm fluids are preferred to cold drinks. And, though they use western silverware, few problems are encountered.

To teach responsibility and cleanliness, each patient must make his own bed, clean his locker and pick-up in his area. In addition to this, each has one chore on the ward such as cleaning the sinks, placing dirty linen in the bag, sweeping the floor or returning food trays to the diet pantry. The spirit of togetherness, and their enthusiasm, is so contagious that most often everyone does his share and more.

When a child first comes to the REPOSE, he is lonely and frightened. Even the presence of the other patients fails to comfort him and we expect, and get, tears for two or three days. However, he is soon caught up in the ward activity, makes many friends, and becomes completely content. Then, fear of the unknown is supplanted by spirit of adventure and their curiosity is boundless. When the day arrives that they must leave, there are tears anew. Several of these will return for follow-up care and there is a striking contrast to their first admission. This time there is no fear, no tears, and the bubbling, energetic child fits readily into the ward pattern with little reorientation.

What happens to our health teaching when our patients return to their homes? We really have no way of knowing. We hope the young carry on what they have learned and the older ones teach the younger in their villages, as they did on the REPOSE. But, with great and optimistic hopes for the future, we see our patients leave with a new set of clothes and, of course their toothbrush, knowing that they are in a better state of health than they have ever enjoyed before.

# AEROSPACE MEDICINE SECTION

## MASS CASUALTY HANDLING ABOARD CARRIER—PART II

Based on a letter from CDR John J. Gordon, MC USN, Medical Officer, USS America (CVA–66), 14 July 1967, concerning the USS Liberty Casualties.

It wears a little thin with all hands after nearly a year of general quarters, drills and lectures on mass casualty handling, and the word is always "this is practice for when the real thing comes, so give it your best no matter how much repetition there seems to be, etc." Well, now we know that all the drills and all the lectures (medical, dental and first aid) and all the practice have paid off magnificently. The following is a brief chronology of the America's participation in the handling of the casualties from the USS Liberty, when she was attacked during the Middle East crisis.

The medical department received word about 1500 on Thursday, 8 June 1967, that the USS Liberty had been attacked. That evening we embarked our general surgeon and two corpsmen via a destroyer to assist the Medical Officer of the Liberty, and we began making preparations to receive casualties. Impromptu changes were made in our mass casualty plan for receiving casualties on the flight deck and all the corpsmen were briefed on what casualty information we had available. We sent messages to the Liberty during the night to get a rough estimate of casualty types and asked if blood was needed, indicating that it could be sent by helo at first light. We then drew 10 pints of O Negative blood and had 30 more typed donors standing by. The second estimate of casualties received from the Liberty was 10 dead, 15 critical injuries and a total of 75 injured.

Casualties began arriving at 1115 on 9 June. By 1415 we had 50 casualties and 9 dead in sick bay. We had stationed one medical officer and several corpsmen with supplies on the flight deck and assigned stretcher bearers to assist with moving the casualties below. We also assigned stretcher bearers to the bomb elevators and on the second deck, so as to reduce waiting period in transit. Our triage system worked very well, and the Aviation Examining Room served much better during the actual casualty than we had expected it would from previous drills. The surgeon began operating at 1500 and completed the fourth major case at 0530

the next morning. We kept two doctors working in the ward which had been opened up by discharging all patients we could on the morning before receiving casualties. The anesthesia training which the Flight Surgeon had received prior to deployment paid off and he did a superb job throughout all the surgical procedures. We opened four abdomens; one required resection of twelve inches of necrotic bowel, another required a right colostomy and the other two were general explorations. Each of these patients had a pneumo- or pneumohemothorax in addition to their abdominal injuries. The surgeon, Doctor Peter Flynn, and I continued to sort and schedule surgical priorities and the entire medical department remained continually busy except for an occasional cup of coffee and sticky bun. Many of the wounds were extensive, having resulted from close range explosions and much shrapnel.

We requested that the mess cooks run our galley, so that all corpsmen could work at medical duties. The x-ray department took 82 films on the first day and a total of 325 films related to the casualties in the first few days. We administered 22 units of blood, encountering no adverse reactions, and the laboratory performed 350 various procedures.

The casualties included 4 fractured skulls, two with shrapnel in the brain. One of these complained only of a "little headache", while the other was in coma when received, but regained conciousness in a few hours. The casualties also included several compound fractures of major bones and one of the femur. Most of the patients were full of shrapnel, including one eye, one lacerated kidney and one suspected ruptured spleen. Three patients had severe powder burns and many had soft tissue contusions and abrasions. During the second and third days we got down to the more minor procedures, and as always had to devote a lot of attention to patient care, especially the post-surgical cases. The fourth day was slower, and each day we seemed to recover more. We began air evacuation of the compound skull fractures early. We had 32 patients to hospitals or returned to duty by the 16th, 6 more to the hospital and duty by the 17th and the last 12 patients to the hospital and duty by the 19th of June. Our major concern, of course, was to air evacuate as the patient's condition allowed, so that we could continue in a fully ready status with this fine hospital of ours.

To sum up, I think the whole thing went off very well from beginning to end. All of our patients did well while aboard here. We have talked a great deal among our group and by keeping a file of ideas, possible improvements and facts as they happened, we feel we have learned some valuable lessons. Reality overwhelmingly proved the value of drills, planning and continual training.

*Editor's Note*: Part I of this series was published in Volume 50, No. 12 of 15 December 1967. Parts III and IV will be concerned with the USS Oriskany fire and with the casualties from an ordnance accident aboard the USS Coral Sea.

## THE THOUSAND AVIATOR STUDY

### Statistical Report of Selected Variables

The Pensacola Study of Naval Aviators, popularly known as the Thousand Aviator Study, began in 1940 when 1,056 student aviators and flight instructors were examined on a variety of physiological and psychological parameters. This longitudinal study has been continued with follow-up examinations in 1951, 1957, and 1963, the latter being the most comprehensive examination to date.

Data described in this report are based on the most recent examination, in which 675 members of the Thousand Aviator group were evaluated in Pensacola. These men ranged in age from 42 to 62 with a mean age of 47. There were 798 survivors of the original group; four could not be located; 31 did not reply to inquiries; and the remaining 88 returned questionnaries but had not been examined at the time this report was prepared.

Data from the Thousand Aviator Study merit special attention for several reasons. First, the original population was young, healthy, and remarkably homogeneous. Furthermore, (1) the spectrum of data gathered is somewhat wider than that of similar studies; (2) all nonstandardized procedures have been carried out by only two investigators, providing a high degree of reliability; and (3) the laboratory data represent an exceptionally large collection of fasting serum specimens from a free-living, nonhospital population.

With the ever-increasing demands for knowledge concerning the relationships among variables considered important in the pathogenesis of coronary heart disease and related circulatory disorders, such a large-scale longitudinal study as that of the Thousand Aviators may provide at least a beginning toward answers to some of these demands.

An awareness of the interrelationships of such factors as cholesterol, blood pressure, and body weight is potentially important not only in the development of control measures for coronary heart disease, but also in the application and interpretation of these measures.

These considerations, combined with the opportunity for perspective gained from an over-all examination of large numbers of related variables, make desirable a detailed statistical description of the information obtained from this group of middle-aged males. The variables are described in terms of distributional statistics and correlation coefficients. It is hoped that these descriptions will be of interest for exploration of relationships not previously apparent, as a reference source for comparative purposes, and for better understanding of other analyses based on data from the Thousand Aviators. The findings are presented only as reference information; comments on possible interpretations are withheld. Subsequent reports will deal with selected aspects of this longitudinal investigation.

(Extracted from: Monograph 12, The Thousand Aviator Study, Distributions and intercorrelations of selected variables, Joint Report of United States Naval Aerospace Medical Institute, United States Public Health Service and National Aeronautics and Space Administration by Oberman, A., Lane, N.E., Mitchell, R.E., and Graybiel, A., 1 September 1965.)

### Smoking History Correlates

During the 1963 follow-up, smoking history information on 675 subjects was obtained by questionnaire and confirmed by interview, together with concurrent data from clinical examinations, laboratory tests, anthropometry, and personal history variables. Two smoking variables were created, Cigarette Amount (CA) and Cigarette Years (CY), each on a scale of 1 to 5 points. From the concurrent data, 62 variables were selected for relevance and general interest to be examined in relation to smoking. Twenty-four of the 62 variables had significant correlations ($p < .05$) with CA, and 16 showed significant relationships to CY. Findings are related briefly to previous research, and problems of cause-effect isolation are mentioned. It is concluded that results in general support previous findings on smoker-nonsmoker differences. Contributions of the study in delineating areas of research for longitudinal investigation are discussed.

(From: The Thousand Aviator Study: Smoking History Correlates of Selected Physiological, Biochemical, and Anthropometric Measures; Joint Report, NAMI–961, 27 April 1966.)

## AEROSPACE EXPERIMENTAL PSYCHOLOGY PROGRAM

A new Naval Officer Billet Classification (NOBC) 0827 entitled "Aerospace Experimental Psychologist" was defined on 22 August 1967 with the promulgation of Change Four to the Manual of Navy Officer Classifications (NAVPERS 15839A).

The Navy's Aerospace Experimental Psychologists held a meeting in Washington, D.C. on 1 September 1967 in conjunction with the American Psychological Association's Annual Convention. The purpose of this meeting was to review the research program at each activity with the intent of promoting increased coordination on problems of common interest and to eliminate any possible duplication of effort.

*Billets*

| | |
|---|---|
| Authorized billets filled | 23 |
| Authorized billets vacant | 4 |
| Total authorized billets | 27 |

*Officers*

| | |
|---|---|
| Occupying authorized billets | 23 |
| In excess (NAVAIRSYSCOM) | 1 |
| Duty under instruction | 5 |
| | 29 |

*Retention*

| Category | *Number* | *Percentage* |
|---|---|---|
| USN | 15 | 52 |
| USNR (Extension ends 1968) | 1 | 4 |
| USNR (Extension ends after 1968) | 3 | 10 |
| USNR (Obligated service ends 1968) | 7 | 24 |
| USNR (Obligated service ends after 1968) | 3 | 10 |

Of the twenty-nine Aerospace Experimental Psychologists presently on active duty nineteen (66%) are either USN or USNR officers who have extended beyond their period of obligated service.

*Recruiting*

| | |
|---|---|
| Inquiries received | 27 |
| Applicants accepted | 7 |
| Applicants rejected | 5 |

During calendar year 1968 it is anticipated that eight officers will be released from active duty. Three applicants were approved and began indoctrination training on 2 January 1968. An additional four applicants have been accepted for the class commencing 5 July 1968.

Recruitment of qualified personnel for the Aerospace Experimental Psychology program is not a problem at this time because of increased draft pressure on graduate students. The increase in the retention rate is probably due to a change in our selection procedures. Previously the applicant with a Doctorate would be accepted rather than an applicant with a Master's degree. Most individuals who enter the Navy with a Ph.D. have fairly firm areas of interest and future plans, and look upon military service as an interruption of these plans and interests. The applicant with a Master's degree, however, usually has a strong desire to obtain his Doctorate but is less rigid in many respects than the Ph.D. applicant. These individuals more readily accept new or different areas of interest and at the same time see an opportunity to obtain a Ph.D. under conditions which cannot be duplicated in civilian life. Ph.D. applicants are still accepted but only if they have unique qualifications.

Two officers have already been nominated to fill two of the four billets vacant and the remaining vacant billets will be filled by June 1968.—AeroMed, BuMed.

## NOTES FROM AEROSPACE PHYSIOLOGY

The semi-annual Quality Assurance Inspection Program on physiological training devices is continuing to gain momentum and support. The first inspections on the West Coast commenced in October 1967 and were completed in November 1967. At the present time results are encouraging, however, many problem areas such as adequate stock levels of spare parts, and qualified maintenance personnel remain to be solved.

A maintenance/operator training course on the 6EQ2 series ejection seat trainers was conducted at the Marine Corps Air Station, Beaufort, South Carolina 27 through 29 November 1967. Fifteen students attended the course.

On 21 November 1967 this Bureau recommended the 9A1B low pressure chamber at the Naval Air Station, Alameda be removed, scheduled for modernization and modification to the configuration of Device 9A1C and allocated to the Naval Air Station, Whidbey Island as a replacement for Device 9A2. This will be the first attempt to move and relocate a large rectangular chamber. This recommendation was made in the interest of cost effectiveness. As a matter of interest a 9A1B chamber cost $30,000 in 1943. The cost of the 9A9 chamber at Pensacola was $125,-000 in 1964.

The low pressure chamber at the Marine Corps Air Station, Cherry Point was grounded 2 September 1967 due to failure of the intercommunication system. A mobile low pressure chamber (Device 9A2) was dispatched from the Naval Air Station, Corpus Christi, Texas and arrived at Cherry Point on 9 October 1967.

Space requirements for the night vision trainer and an adjoining classroom were submitted for inclusion in the plans for the proposed Dispensary at the Naval Air Station, Key West, Florida for FY 1969.

The proposal for a new Naval Hospital at the Naval Air Station, Corpus Christi, Texas for FY 1969 includes spaces for an Aerospace Physiology Training Unit.

The current inventory of physiological training devices includes thirty-two low pressure chambers, and thirty-three ejection seat trainers. Of the low pressure chambers, sixteen are utilized exclusively for training, six are utilized for research, development, test and evaluation studies, one is under procurement and nine are inactive. Of the ejection seat trainers, thirty-one are operational and two are undergoing modernization/modification.—Aero Med, BuMed.

## MARTIN-BAKER EJECTION KILOTURION

Martin-Baker ejection seats are in use in Army, Navy, and Air Force aircraft. Information on emergency escape statistics indicates that the 1000th ejection by U.S. Forces using Martin-Baker seats was made on 15 December 1967. It was coincidental that both the first and the 1000th ejection were made from the same type aircraft, TF–9J Navy jet trainer, at the same airbase, Naval Auxiliary Air Station, Kingville, Texas. The first ejection was made on 25 September 1958 and since then the Martin-Baker escape systems in twelve different aircraft have achieved a success rate of 88%.

The Naval Air Systems Command is currently improving several Martin-Baker escape systems by incorporating a rocket propulsion system to provide an escape capability at zero speed at zero

altitude to reduce injuries and achieve a better success rate.—NavAirSystems (AIR–5312C).

## SECOND OPERATIONAL USE OF F–111 ESCAPE CAPSULE

On 2 January 1968 the second operational use of the capsule module was made for escape from an F–111A due to fire in flight. The escape was made at 290 knots at about 9000 ft. in the vicinity of Edwards, AFB.

The fire was not in the module but in the tunnel under the module and at the bulkhead in back of it in the vicinity of the fuel cell. The fire burned into the lines which actuate the flotation bags and also those which lead into the drogue chute gun. The drogue chute gun did not explode as was first believed but the drogue chute was not deployed. As a result the module was not stabilized prior to main parachute deployment. Although some of the module separation lines were burned, no difficulty was experienced in capsule separation from the aircraft.

There was some acrid smoke in the cockpit as in the previous escape from the firing of the separation rocket.

The ground impact of the capsule was severe, resulting in minor back injury to the co-pilot. He is, however, still on flight status. There was a strong side wind drifting the capsule to the right so the capsule impacted on the right side and rolled over. The crew exited the capsule without difficulty.

The severity of the module impact was due, in part, to the fact that the descent speed of the capsule under the parachute at the 4,000 ft. elevation where the capsule impacted, was greater than it would have been at sea level.—NavAirSystems (AIR–5312C).

## CHANGES IN FAA FORMS

FAA Form 1004 is now obsolete: On May 1, 1967, FAA Form 1004 was replaced by FAA Form 8500–8, "Application for Medical Certificate." You were asked to destroy all editions of FAA Form 1004 you had on hand. The Aeromedical Certification Branch, AC–130, reports they are still receiving some of the obsolete FAA Form 1004. If for some reason you do not have a supply of the new FAA Form 8500–8, "Application for Medical Certificate," please request a supply from your Regional Flight Surgeon (in case of military or International AME, from the Aeromedical Certification Branch, AC–135).

Voided Forms 8500–8: The Regional Flight Surgeons' offices, as well as the Aeromedical Certification office in Oklahoma City, are receiving inquiries from AMEs regarding disposition of voided copies of the examination Forms 8500–8. Voided copies of these forms (for which a new form has been prepared) may be defaced to prevent their reuse and destroyed in the AME's office. It is not necessary to mail the voided copies to Oklahoma City. Since the forms are prenumbered, it is reasonable to assume that an accounting of each number is to be made. However, this is not the case. The forms are prenumbered merely because it is necessary that each student pilot certificate have a number.—Extract from Federal Air Surgeons' Medical Bulletin, 67–2, Sept 1967.

## TOP STUDENT FLIGHT SURGEON

LT William R. Davis, MC USNR, was presented the Navy Surgeon General Award from RADM H. H. Eighmy, MC USN, CO, NAMC, in graduation ceremonies December 14 at the Naval Aerospace Medical Institute, Pensacola, Florida. LT Davis, outstanding graduate in academics and leadership in Flight Surgeon Class 116, is from Hemet, California. He received his M.D. from Loma Linda University Medical School in California. LT Davis has a private pilot's license. He is being assigned to Carrier Air Wing FIVE at Miramar, California.—"Capsule" Dec 1967.

## AVIATION PERSONAL AND SURVIVAL EQUIPMENT TEAM (APSET)

As aerospace medical advisor for flight and survival equipment for DCNO (AIR), CAPT M.D. Courtney, MC USN, chaired meetings of the Aviation Personal and Survival Equipment Team (APSET) in August and in December held at the Naval Air Systems Headquarters. These meetings, attended by representatives from operational, training, RTD&E, procurement and supply activities of the Navy, as well as representatives of the Army, Air Force and Coast Guard, are held for the purpose of determining new or changed requirements for subject equipment and the forwarding of appropriate recommendations concerning such requirements to the DCNO (AIR). The team has been functioning for three years, but was not formally established till 11 August 1967 as an intra-Navy committee under the authority of OPNAVINSTRUCTION 5420.59.—AeroMed, BuMed.

# EDITOR'S SECTION

## ANGINA PECTORIS

Two middle-aged men, who, just six months ago, had to stop nearly all physical activity due to staggering heart pain (angina pectoris), have now resumed nearly normal activity because of a new technique applied by a research team at the National Heart Institute, one of the eight National Institutes of Health.

In each patient, investigators surgically implanted an electronic device that the patient switches on to stimulate certain nerves in the neck that are responsible for slowing down heart action.

In addition to alleviating severe anginal pain, the technique may, by allowing increased physical activity, encourage the development of new blood channels to blood-starved areas of the heart, thus cutting down the number of painful attacks by eliminating their cause.

This research, reported in the current issue of the *New England Journal of Medicine*, was performed by Drs. Eugene Braunwald, Stephen Epstein, Gerald Glick, Andrew Wechsler, and Nina Braunwald of the National Heart Institute's Cardiology Branch.

Both patients had previously suffered a myocardial infarction, or typical heart attack in which a portion of the heart muscle is deprived of its blood supply and dies.

The excruciating, incapacitating pains of angina pectoris, which are a consequence of inadequate oxygen supply to the heart muscle, had forced the two men, a 54-year-old artist and a 51-year-old drug salesman to leave their jobs and lead sedentary lives. They suffered severe pain triggered by exposure to cold, emotional upset, coitus, ingestion of large meals, and even the most moderate exercise, for example, bathing.

Typically, therapy for angina pectoris either increases coronary blood flow, thus bringing more oxygen to the heart, or decreases the heart's need for oxygen. In these cases, however, increasing blood flow was not the solution, because both men had hardening of the arteries (atherosclerosis) which limited the ability of their coronary arteries to dilate and thus carry more blood. Drugs to reduce oxygen requirements were not the solution because they acted too slowly and incompletely in these patients. A method to decrease myocardial oxygen requirements seemed the better alternative. Previous experimental studies at the NHI had demonstrated that oxygen needs are directly related to heart rate, to tension in the heart muscle and to pressure in the ventricles of the heart. If these factors are reduced, the heart's oxygen needs are also reduced.

The NHI research team accomplished this in both patients by equipping them with electronic apparatus that stimulates the carotid sinus nerves. The electrical stimulus is generated by a small transmitter worn outside the body; transmitted by wire to a light-weight disc-shaped coil; beamed through the intact chest wall to a receiving unit implanted just under the skin; and finally carried via wire electrodes to carotid sinus nerves high up in either side of the neck.

### Background Statement

The carotid sinus nerves, located in the neck in a blood pressure-sensitive area of the carotid arteries normally maintain blood pressure within a narrow range.

When blood pressure rises above or falls below this range, the carotid sinus detects the changes and tends to bring blood pressure back within the normal range via the carotid sinus nerves. These act through the autonomic nervous system to bring about appropriate alterations in heart rate, heart output and blood vessel tone (vessel diameter).

When the carotid sinus is stimulated by electrical impulses, the sinus "reads" the blood pressure as being above normal and thus compensates by reducing blood pressure and blood vessel tone. In this way it reduces heart work and hence heart oxygen requirements, and relieves anginal pain.

One of the men to receive the stimulation unit chose the type equipped with a button which produces carotid sinus nerve stimulation for one minute, after being depressed momentarily. He depresses the button as soon as anginal pains occur and reports that pain subsides in just seconds. Though he still has attacks as frequently as before the transmitter was installed, the pain no longer inhibits his activities.

The other man chose a transmitter which is activated by an on-off switch. He uses the stimulator to prevent pain, as well as to alleviate it, by pushing the button before he engages in activity that once triggered anginal pain. The longest he has ever activated the stimulator is from 30–40 minutes at a time.

Prior to receiving the stimulator device, both men were under typical drug therapy for angina, including nitroglycerine and propranolol. One of the men also had to rely on a narcotic, Demerol, for blunting very severe pains. Now, with the device implanted, neither uses any medication at all and both report that they prefer the stimulator to the drugs.

The only side-effects the men experience is a slight difficulty in speaking which they attribute to the surgery and which seems to be decreasing. When the stimulator is activated, they receive a mild tingling sensation in the neck at the site of the carotid sinus. Both of the men say they actually like this sensation, as it assures them that the stimulator is operating properly.

In laboratory tests, the research team has found that carotid nerve stimulation enables the men to increase activity 15-fold in duration and raise considerably the intensity of exercise. With the stimulator activated, the men stopped exercising, not because of anginal pain, but because of fatigue or because researchers terminated the test.

In the absence of carotid sinus nerve stimulation, as the intensity of exercise was increased, arterial pressure and heart rate increased progressively until angina developed. When the stimulator was activated, arterial pressure and heart rate decreased within 3–4 heart beats. When the stimulator was begun prior to exercise, arterial pressure and heart rate was lower throughout the exercise period.

Other studies showed that though the stimulator reduced arterial pressure and heart rate more effectively than either nitroglycerine or propranolol, the use of the stimulator and propranolol together allowed somewhat higher rates and duration.

In these two patients, carotid nerve stimulation seems superior to nitroglycerine treatment for several reasons. It is more rapid in relieving anginal pain so that the men are not forced to interrupt activity that precipitated the angina. Stimulation appears more reliable in aborting each angina episode and is not accompanied by nitroglycerine side-effects such as headache, pounding pulse, and faintness.

The stimulator seems more desirable physiologically, because it alters nerve activity influencing heart action only intermittently—during angina attacks—whereas the effects of drugs such as propranolol persist for hours.

In addition, Dr. Eugene Braunwald believes that the stimulator may alter favorably the natural history of angina pectoris by allowing formerly sedentary patients to initiate a program of increasing physical activity. This activity may gradually force open collateral arteries—accessory arteries to reach areas of the heart that would otherwise be deprived of oxygen-carrying blood.

The selection of patients for implantation of carotid sinus nerve stimulation units must be approached with caution, according to Dr. Eugene Braunwald. Suitable candidates are those with long-standing, incapacitating angina in whom a sufficient increase in exercise tolerance can be demonstrated when nitroglycerine and propranolol are given. The candidate should show no signs or symptoms of carotid artery insufficiency or preinfarction syndrome (signs of impending heart attack).—USDHEW, National Heart Institute, Bethesda, Md.

## ESTABLISHMENT OF A CLEFT PALATE CLINIC AT THE CHELSEA NAVAL HOSPITAL

The Naval Hospital, Chelsea, Massachusetts, was recently authorized by the Bureau of Medicine and Surgery to establish a Cleft Palate Clinic. This is believed to constitute the first such clinic in the Navy and one of the very few in the United States. Its establishment represents a significant advance in the care and treatment of the cleft palate patient, and provides a well coordinated program of care which includes not only the initial surgery, but repair of dental defects, otolaryngologic care, speech therapy, follow-up cosmetic procedures, prosthodontistry and oral surgery for residuals.

Prior to the establishment of this clinic the various specialists who provided treatment to the cleft palate patient tended to perform only a part of the total care, and there was very limited coordination of the overall treatment plan. With the establishment of this clinic a well coordinated and effective program has evolved with clearly defined responsibilities for each specialist.

CAPT Tracy D. Cuttle, MC USN, Commanding Officer of the Chelsea Naval Hospital, has indicated that this program has produced an extremely fine affect upon the morale of those parents whose children are receiving care in the clinic. Additionally, observation of the coordinated efforts of the various specialist, by the family, is reported to

have significantly alleviated their anxieties and assisted immeasurably in assuring the parents that they are doing everything possible for the care of their child.

Activities desiring information concerning the establishment and operation of this clinic are encouraged to contact the Commanding Officer, Naval Hospital, Chelsea, Massachusetts 02150.

## PEDIATRIC SEMINAR

The Fourth Annual Uniformed Services' Pediatric Seminar will be held at the National Naval Medical Center from 6–8 March 1968. An interesting program is planned. There will be a full day on "Neonatology" followed by half-day sessions on "Hematology," "The Exceptional Child," "Immunology and Allergy," and "Pediatric Radiology." There will also be an evening session for research papers. All service pediatricians are invited to attend. A preliminary program will be forwarded to all Army, Navy, Air Force, and Public Health Hospitals in January. Further information may be obtained by writing to Course Director, Uniformed Services' Pediatric Seminar, National Naval Medical Center, Bethesda, Maryland 20014.

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